JC03 Rec'd PCT/PTO 24 AUG 2001

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 USC 371	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY DOCKET NO. 440500/PALL
		U.S. APPLICATION NO. 09/914166
INTERNATIONAL APPLICATION NO. PCT/US00/04785	INTERNATIONAL FILING DATE 25 FEB 2000	PRIORITY DATE CLAIMED 25 FEB 1999

TITLE OF INVENTION
CHROMATOGRAPHY DEVICES AND FLOW DISTRIBUTOR ARRANGEMENTS USED IN CHROMATOGRAPHY ARRANGEMENTS

APPLICANT(S) FOR DO/EO/US
PALL CORPORATION

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 USC 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 USC 371.
3. ☒ This is an express request to begin national examination procedures (35 USC 371(f)).
4. ☐ The US has been elected by the expiration of 19 months from the priority date (PCT Article 31).
5. ☒ A copy of the International Application as filed (35 USC 371(c)(2))
   a. ☐ is attached hereto (required only if not communicated by the International Bureau).
   b. ☒ has been communicated by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International Application as filed (35 USC 371(c)(2)).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 USC 371(c)(3))
   a. ☐ are attached hereto (required only if not communicated by the International Bureau).
   b. ☐ have been communicated by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 USC 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 USC 371(c)(4)).
10. ☐ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 USC 371(c)(5)).
11. Nucleotide and/or Amino Acid Sequence Submission
   a. ☐ Computer Readable Form (CRF)
   b. Specification Sequence Listing on:
      i. ☐ CD-ROM or CD-R (2 copies); or
      ii. ☐ Paper Copy
   c. ☐ Statement verifying identity of above copies

Items 12 to 19 below concern other document(s) or information included:

12. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
    ☐ Form PTO-1449
    ☐ Copies of Listed Documents
13. ☐ An assignment for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
14. ☒ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.
15. ☐ A substitute specification.
16. ☐ A change of power of attorney and/or address letter.
17. ☒ Application Data Sheet Under 37 CFR 1.76
18. ☒ Return Receipt Postcard
19. ☒ Other items or information: International Publication No. WO 00/50144 including the International Search Report, and International Preliminary Examination Report (Forms PCT/IPEA/416 and PCT/IPEA/409)

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U.S. APPLICATION NO. 09/914166	INTERNATIONAL APPLICATION NO. PCT/US00/04785	ATTORNEY DOCKET NO. 440500/PALL

	CALCULATIONS	PTO USE ONLY
20. ☒ The following fees are submitted: **Basic National Fee (37 CFR 1.492(a)(1)-(5)):** Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO .... $1,000.00 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO .... $ 860.00 International preliminary examination fee (37 CFR 1.482) paid to USPTO, but international search fee (37 CFR 1.445(a)(2))paid to USPTO .... $ 710.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4)........................ $ 690.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1) to (4) .... $ 100.00		
ENTER APPROPRIATE BASIC FEE AMOUNT=	$100.00	
Surcharge of $130.00 for furnishing the National fee or oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date	$	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	CALCULATIONS	PTO USE ONLY
Total Claims	50 -20=	30	x $ 18.00	$540.00	
Independent Claims	6 - 3 =	3	x $ 80.00	$240.00	
☐ Multiple Dependent Claim(s) (if applicable)			+$270.00	$	
TOTAL OF ABOVE CALCULATIONS=				$	
☐ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.				$	
SUBTOTAL=				$	
Processing fee of **$130.00** for furnishing English Translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date.				$	
TOTAL NATIONAL FEE=				$	
Fee for recording the enclosed assignment. The assignment must be accompanied by an appropriate cover sheet. **$40.00** per property +				$	
TOTAL FEE ENCLOSED=				$880.00	
				Amount to be: refunded	$
				charged:	$

a. ☒ A check in the amount of $880.00 to cover the above fee is enclosed.

b. ☐ Please charge Deposit Account No. 12-1216 in the amount of $ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 12-1216. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

23548
PATENT TRADEMARK OFFICE

John M. Belz, Registration No. 30,359
One of the Attorneys for Applicant(s)

24 Aug 2001
Date

PATENT
Attorney Docket No. 440500/PALL

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Hurwitz et al.

Art Unit: Unknown

United States National Stage of International Application No. PCT/US00/04785 Filed February 25, 2000

Examiner: Ernest G. Therkorn

For: CHROMATOGRAPHY DEVICES AND FLOW DISTRIBUTOR ARRANGEMENTS USED IN CHROMATOGRAPHY DEVICES

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Prior to the examination of, and calculation of the filing fee for, the above-identified patent application, please enter the following amendments and consider the following remarks.

IN THE CLAIMS:

Replace the indicated claims with:

3. (Amended) The flow distributor arrangement according to claim 1, wherein the tapered space has a tapered end and a flat end.

6. (Amended) The flow distributor arrangement according to claim 1, wherein the tapered space is free of structures.

7. (Amended) The flow distributor arrangement according claim 1, wherein the flow distributor is arranged to reduce flow disturbances as fluid enters or exits the tapered space.

8. (Amended) The flow distributor arrangement according to claim 1 including another fluid distributor disposed in the flow path between the tapered space and the second passage.

11. (Amended) The flow distributor arrangement according to claim 9, wherein the tapered space has a tapered end and a flat end.

14. (Amended) The flow distributor arrangement according to claim 9, wherein the tapered space is substantially free of structures.

15. (Amended) The flow distributor arrangement according to claim 9, wherein the first flow distributor is capable of reducing flow disturbances as fluid enters or exits the tapered space.

18. (Amended) The chromatography device according to claim 16, wherein the tapered space has a tapered end and a flat end.

21. (Amended) The chromatography device according to claim 16, wherein the tapered space is substantially free of structures.

22. (Amended) The chromatography device according to claim 16 including a stationary separation medium holder including first and second plates, the first plate including the inlet and the second plate including the outlet, the porous medium module being disposed between the first and second plates.

24. (Amended) The chromatography device according to claim 22, wherein the porous flow distributor is mounted to the first plate.

25. (Amended) The chromatography device according to claim 16, wherein the flow distributor is arranged to reduce flow disturbances as fluid enters the tapered space from the inlet.

26. (Amended) The chromatography device according to claim 16 wherein the flow distributor comprises a first flow distributor and wherein the flow distributor arrangement further includes a second porous flow distributor disposed in the flow path between the tapered space and the porous media.

28. (Amended) The chromatography device according to claim 26, wherein the first porous flow distributor abuts the second porous flow distributor.

29. (Amended) The chromatography device according to claim 26, wherein the first porous flow distributor is spaced from the second porous flow distributor.

30. (Amended) The chromatography device according to claim 26, wherein the second porous flow distributor is adapted to enhance uniform fluid flow.

31. (Amended) The chromatography device according to claim 26, wherein the second porous flow distributor is disposed in the porous medium module.

32. (Amended) he chromatography device according to claim 26, wherein the second porous flow distributor is disposed in the tapered space.

33. (Amended) The chromatography device according to claim 16, wherein the flow distributor arrangement is a first flow distributor arrangement and is disposed in the flow path between the porous media and the inlet, and wherein the chromatography device includes a second flow distributor arrangement disposed in the flow path between the porous media and the outlet.

36. (Amended) The chromatography device according to claim 34 wherein the porous flow distributor of the second flow distributor arrangement comprises a first porous flow distributor and wherein the second flow distributor arrangement further includes a second porous flow distributor disposed in the flow path between the porous media and the outlet.

40. (Amended) A chromatography device according to claim 38 wherein the tapered space includes inner and outer tapered sections.

42. (Amended) A chromatography device according to claim 38 wherein the flow distributor arrangement includes another porous flow distributor disposed in the flow path between the tapered space and said one of the inlet or the outlet.

43. (Amended) A chromatography device according to claim 38 wherein the flow distributor is the sole flow distributor of the flow distributor arrangement.

47. (Amended) A flow distributor arrangement as claimed in claim 44 wherein the first and second tapered sections have different tapers.

49. (Amended) A flow distributor arrangement as claimed in claim 44 wherein the tapered space further includes a flat disposed between the first and second tapered sections.

REMARKS

The foregoing Amendment corrects multiple dependencies and conforms the claims to United States practice.

Respectfully submitted,

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PATENT
Attorney Docket No. 440500/PALL

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Hurwitz et al.

Art Unit: Unknown

Examiner: Ernest G. Therkorn

United States National Stage of
International Application
No. PCT/US00/04785
Filed February 25, 2000

For: CHROMATOGRAPHY DEVICES AND FLOW DISTRIBUTOR ARRANGEMENTS USED IN CHROMATOGRAPHY DEVICES

AMENDMENTS TO SPECIFICATION, CLAIMS AND ABSTRACT MADE VIA PRELIMINARY AMENDMENT

Amendments to existing claims:

3. (Amended) The flow distributor arrangement according to claim 1 ~~or 2~~, wherein the tapered space has a tapered end and a flat end.

6. (Amended) The flow distributor arrangement according to ~~any one of the preceding claims~~ claim 1, wherein the tapered space is free of structures.

7. (Amended) The flow distributor arrangement according ~~to any one of the preceding claims~~ claim 1, wherein the flow distributor is arranged to reduce flow disturbances as fluid enters or exits the tapered space.

8. (Amended) The flow distributor arrangement according to ~~any one of the preceding claims~~ claim 1 including another fluid distributor disposed in the flow path between the tapered space and the second passage.

11. (Amended) The flow distributor arrangement according to claim 9 ~~or 10~~, wherein the tapered space has a tapered end and a flat end.

15. (Amended) The flow distributor arrangement according to ~~any one of claims 9 to 14~~ claim 9, wherein the first flow distributor is capable of reducing flow disturbances as fluid enters or exits the tapered space.

18. (Amended) The chromatography device according to claim 16 ~~or 17~~, wherein the tapered space has a tapered end and a flat end.

21. (Amended) The chromatography device according to ~~any one of claims 16 to 20~~ claim 16, wherein the tapered space is substantially free of structures.

22. (Amended) The chromatography device according to ~~any one of claims 16 to 21~~ claim 16 including a stationary separation medium holder including first and second plates, the first plate including the inlet and the second plate including the outlet, the porous medium module being disposed between the first and second plates.

24. (Amended) The chromatography device according to claim 22 ~~or 23~~, wherein the porous flow distributor is mounted to the first plate.

25. (Amended) The chromatography device according to ~~any one of claims 16 to 23~~ claim 16, wherein the flow distributor is arranged to reduce flow disturbances as fluid enters the tapered space from the inlet.

26. (Amended) The chromatography device according to ~~any one of claims 16 to 25~~ claim 16 wherein the flow distributor comprises a first flow distributor and wherein the flow distributor arrangement further includes a second porous flow distributor disposed in the flow path between the tapered space and the porous media.

28. (Amended) The chromatography device according to claim 26 ~~or 27~~, wherein the first porous flow distributor abuts the second porous flow distributor.

29. (Amended) The chromatography device according to claim 26 ~~or 27~~, wherein the first porous flow distributor is spaced from the second porous flow distributor.

30. (Amended) The chromatography device according to ~~any one of claims 26 to 29~~ claim 26, wherein the second porous flow distributor is adapted to enhance uniform fluid flow.

31. (Amended) The chromatography device according to ~~any one of claims 26 to 30~~ claim 26, wherein the second porous flow distributor is disposed in the porous medium module.

32. (Amended) he chromatography device according to ~~any one of claims 26 to 30~~ claim 26, wherein the second porous flow distributor is disposed in the tapered space.

33. (Amended) he chromatography device according to ~~any one of claims 16 to 32~~ claim 16, wherein the flow distributor arrangement is a first flow distributor arrangement and is disposed in the flow path between the porous media and the inlet, and wherein the chromatography device includes a second flow distributor arrangement disposed in the flow path between the porous media and the outlet.

36. (Amended) The chromatography device according to claim 34 ~~or 35~~ wherein the porous flow distributor of the second flow distributor arrangement comprises a first porous flow distributor and wherein the second flow distributor arrangement further includes a second porous flow distributor disposed in the flow path between the porous media and the outlet.

40. (Amended) A chromatography device according to claim 38 ~~or 39~~ wherein the tapered space includes inner and outer tapered sections.

42. (Amended) A chromatography device according to ~~any of claims 38-41~~ claim 38 wherein the flow distributor arrangement includes another porous flow distributor disposed in the flow path between the tapered space and said one of the inlet or the outlet.

43. (Amended) A chromatography device according to ~~any of claims 38-41~~ claim 38 wherein the flow distributor is the sole flow distributor of the flow distributor arrangement.

47. (Amended) A flow distributor arrangement as claimed in ~~any of claims 44-46~~ claim 44 wherein the first and second tapered sections have different tapers.

49. (Amended) A flow distributor arrangement as claimed in ~~any of claims 44-48~~ claim 44 wherein the tapered space further includes a flat disposed between the first and second tapered sections.

PATENT
Attorney Docket No. 440500/PALL

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Hurwitz et al.

Art Unit: Unknown

Examiner: Ernest G. Therkorn

United States National Stage of
International Application No. PCT/US00/04785
Filed February 25, 2000

For: CHROMATOGRAPHY DEVICES AND FLOW DISTRIBUTOR ARRANGEMENTS USED IN CHROMATOGRAPHY DEVICES

PENDING CLAIMS AFTER ENTRY OF PRELIMINARY AMENDMENT

1. A flow distributor arrangement for distributing fluid flow in a chromatography device along a flow path between a first passage having a first flow area and a second passage having a second flow area larger than the first flow area, the flow distributor arrangement comprising:
a tapered space in the flow path between the first passage and the second passage, the tapered space being substantially free of any structures; and
a porous flow distributor disposed in the flow path and fluidly coupled to the tapered space wherein fluid flowing between the tapered space and the first passage passes through the porous flow distributor.

2. The flow distributor arrangement according to claim 1, wherein the tapered space has an outer periphery, and the tapered space is thicker at a location adjacent to the first passage and thinner at the outer periphery.

3. The flow distributor arrangement according to claim 1, wherein the tapered space has a tapered end and a flat end.

4. The flow distributor arrangement according to claim 3, wherein the tapered end of the tapered space has a straight taper.

6. The flow distributor arrangement according to claim 1, wherein the tapered space is free of structures.

7. The flow distributor arrangement according claim 1, wherein the flow distributor is arranged to reduce flow disturbances as fluid enters or exits the tapered space.

8. The flow distributor arrangement according to claim 1 including another fluid distributor disposed in the flow path between the tapered space and the second passage.

9. A flow distributor arrangement for distributing fluid flow in a chromatography device along a flow path between a first passage having a first flow area and a second passage having a second flow area larger than the first flow area, the flow distributor arrangement comprising:

a first porous flow distributor arranged to distribute fluid from or to the first passage; a second porous flow distributor arranged to distribute fluid to or from the second passage; and

a tapered space fluidly coupled to the first and second porous flow distributors to direct at least a portion of the fluid between the first and second flow distributors.

10. The flow distributor arrangement according to claim 9, wherein the tapered space has an outer periphery, and the tapered space is thicker at a location adjacent to the first passage and thinner at the outer periphery.

11. The flow distributor arrangement according to claim 9, wherein the tapered space has a tapered end and a flat end.

12. The flow distributor arrangement according to claim 11, wherein the tapered end of the tapered space has a straight taper.

13. The flow distributor arrangement according to claim 11, wherein the tapered end of the tapered space has a curved taper.

14. The flow distributor arrangement according to claim 9, wherein the tapered space is substantially free of structures.

15. The flow distributor arrangement according to claim 9, wherein the first flow distributor is capable of reducing flow disturbances as fluid enters or exits the tapered space.

16. A chromatography device comprising:

an inlet and an outlet;

a porous medium module including a stack of porous media disposed in a flow path between the inlet and the outlet, the porous media having a flow area larger than a flow area of at least one of the inlet and the outlet; and

a flow distributor arrangement disposed in the flow path between the porous media and said one of the inlet and the outlet, the flow distributor arrangement including a tapered space and a porous flow distributor the tapered space being disposed in the flow path between the porous media and said one of the inlet and the outlet and being substantially free of structures, and the porous flow distributor is fluidly coupled to the tapered space wherein fluid flowing between the tapered space and said one of the inlet and the outlet passes through the porous flow distributor.

17. The chromatography device according to claim 16, wherein the tapered space has an outer periphery, and the tapered space is thicker at a location adjacent to the inlet and thinner at the outer periphery.

18. The chromatography device according to claim 16, wherein the tapered space has a tapered end and a flat end.

19. The chromatography device according to claim 18, wherein the tapered end of the tapered space has a straight taper.

20. The chromatography device according to claim 19, wherein the tapered end of the tapered space has a curved taper.

21. The chromatography device according to claim 16, wherein the tapered space is substantially free of structures.

22. The chromatography device according to claim 16 including a stationary separation medium holder including first and second plates, the first plate including the inlet and the second plate including the outlet, the porous medium module being disposed between the first and second plates.

23. The chromatography device according to claim 22, wherein the tapered space includes a recess in the first plate.

24. The chromatography device according to claim 22, wherein the porous flow distributor is mounted to the first plate.

25. The chromatography device according to claim 16, wherein the flow distributor is arranged to reduce flow disturbances as fluid enters the tapered space from the inlet.

26. The chromatography device according to claim 16 wherein the flow distributor comprises a first flow distributor and wherein the flow distributor arrangement further includes a second porous flow distributor disposed in the flow path between the tapered space and the porous media.

27. The chromatography device according to claim 26, wherein the tapered space includes a recess in the second porous flow distributor.

28. The chromatography device according to claim 26, wherein the first porous flow distributor abuts the second porous flow distributor.

29. The chromatography device according to claim 26, wherein the first porous flow distributor is spaced from the second porous flow distributor.

30. The chromatography device according to claim 26, wherein the second porous flow distributor is adapted to enhance uniform fluid flow.

31. The chromatography device according to claim 26, wherein the second porous flow distributor is disposed in the porous medium module.

32. he chromatography device according to claim 26, wherein the second porous flow distributor is disposed in the tapered space.

33. The chromatography device according to claim 16, wherein the flow distributor arrangement is a first flow distributor arrangement and is disposed in the flow path between the porous media and the inlet, and wherein the chromatography device includes a second flow distributor arrangement disposed in the flow path between the porous media and the outlet.

34. The chromatography device according to claim 33, wherein the second flow distributor arrangement includes a tapered space and a porous flow distributor fluidly coupled to the tapered space, the tapered space of the second flow distributor arrangement being

disposed in the flow path between the porous media and the outlet, wherein fluid flowing between the tapered space of the second flow distributor arrangement and the inlet passes through the porous flow distributor of the second flow distributor arrangement.

35. The chromatography device according to claim 34, wherein the tapered space of the second flow distributor arrangement is substantially free of structures.

36. The chromatography device according to claim 34 wherein the porous flow distributor of the second flow distributor arrangement comprises a first porous flow distributor and wherein the second flow distributor arrangement further includes a second porous flow distributor disposed in the flow path between the porous media and the outlet.

37. The chromatography device according to claim 36 wherein first porous flow distributor of the second flow distributor arrangement is mounted to the second plate and the second porous flow distributor of the second flow distributor arrangement is disposed in the porous medium module.

38. A chromatography device comprising:

an inlet and an outlet;

a porous medium module including a stack of porous media disposed in a flow path between the inlet and the outlet, the porous media having a flow area larger than a flow area of at least one of the inlet and the outlet; and

a flow distributor arrangement disposed in the flow path between the porous media and said one of the inlet and the outlet, the flow distributor arrangement including a tapered space and a porous flow distributor fluidly coupled to the tapered space, wherein the tapered space is disposed in the flow path between the porous media and said one of the inlet and the outlet and wherein the porous flow distributor is disposed in the flow path between the tapered space the porous media, the porous flow distributor being integrally secured to the porous medium module.

39. A chromatography device according to claim 38 wherein the tapered space is substantially free of structures.

40. A chromatography device according to claim 38 wherein the tapered space includes inner and outer tapered sections.

41. A chromatography device according to claim 40 wherein the tapered space includes a flat disposed between the inner and outer tapered sections and wherein the flow

distributor arrangement includes supports extending from the flat toward the porous medium module.

42. A chromatography device according to claim 38 wherein the flow distributor arrangement includes another porous flow distributor disposed in the flow path between the tapered space and said one of the inlet or the outlet.

43. A chromatography device according to claim 38 wherein the flow distributor is the sole flow distributor of the flow distributor arrangement.

44. A flow distributor arrangement for distributing fluid flow in a chromatography device along a flow path between a first passage and a second passage, one of the passages having a larger flow area than the other passage, the flow distributor arrangement comprising:

a tapered space in the flow path between the first passage and the second passage, the tapered space including a first tapered section and a second tapered section disposed outwardly of the first tapered section; and

a porous flow distributor disposed in the flow path and fluidly coupled to the tapered space.

45. A flow distributor arrangement as claimed in claim 44 wherein the porous flow distributor is disposed in the fluid flow path between the tapered space and the first passage.

46. A flow distributor arrangement as claimed in claim 44 wherein the porous flow distributor is disposed in the fluid flow path between the tapered space and the second passage.

47. A flow distributor arrangement as claimed in claim 44 wherein the first and second tapered sections have different tapers.

48. A flow distributor arrangement as claimed in claim 47 wherein the first and second tapered sections respectively comprise inner and outer tapered sections, the inner tapered section having a steeper slope than the outer tapered section.

49. A flow distributor arrangement as claimed in claim 44 wherein the tapered space further includes a flat disposed between the first and second tapered sections.

50. A chromatography device comprising:

an inlet and an outlet defining a fluid flow path;

a porous medium module include a stack of porous media having a first end and a porous medium support supporting the first end of the stack of porous media, the porous medium module being disposed in the fluid flow path between the inlet and the outlet; and

a flow distributor arrangement disposed in the fluid flow path between the porous medium support and one of the inlet and the outlet, the flow distributor arrangement including a tapered space and a porous flow distributor fluidly coupled to the tapered space.

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CHROMATOGRAPHY DEVICES AND FLOW DISTRIBUTOR ARRANGEMENTS USED IN CHROMATOGRAPHY DEVICES

The present application claims the benefit of priority of United States Patent Application No. 60/121,701 filed on February 25, 1999 and United States Patent Application No. 60/168,750 filed on December 6, 1999. United States Applications No. 60/121,701 and No. 60/168,750 and all other patent applications, patents, and publications listed in the present application are incorporated by reference.

FIELD OF THE INVENTION

This invention is related to chromatography devices and flow distributor arrangements used in chromatography devices.

BACKGROUND OF THE INVENTION

Chromatography is a term applied to a variety of separation techniques and can be classified in several ways, including gas chromatography and liquid chromatography, such as ion exchange chromatography, affinity chromatography, size exclusion chromatography, etc. The term "chromatography" as used herein includes any conventional chromatographic and/or adsorptive separation technique.

A chromatography process may be illustrated using ion exchange chromatography. Ion exchange chromatography usually involves a two-step process for separating components from the fluid containing the components. First, a test sample including a fluid and the components contained therein is passed through a chromatography device such as a chromatography column. The chromatography device usually includes a stationary separation medium, such as a bed of porous beads or a stack of porous membranes or sheets, for separating or isolating the components from the fluid. As the test sample passes through the chromatography device the components become associated with the separation medium by any of a variety of chemical and/or physical processes. For example, the components may become chemically or physically attached to the

separation medium. In the case of ion exchange chromatography, the components may be attached to the medium by electric charge.

Second, after the test sample has passed through the separation medium and the components in the test sample are attached to the separation medium, a continuous stream of an eluent is passed through the separation medium, whereupon the components attached to the separation medium are released to the eluent. In ion exchange chromatography, the eluent may be a salt solution, ions of which replace the components on the separation medium. Typically, the salt concentration is varied with time either gradually using gradient elution or suddenly as in step or isochratic elution. Because different components have different affinities for the separation medium, the time at which each component is released into the eluent may vary. For example, in gradient elution where the salt concentration increases with time, the component having the least affinity for the separation medium will be released into the eluent first, and the component having the most affinity for the separation medium will be released into the eluent last. The presence of each component in the eluent is generally detected by measuring changes in the physico-chemical properties (for example, by measuring the adsorption of light at 280 nm) of the eluent as the eluent exits the separation medium. A plot of the changes of these properties versus time will exhibit response peaks corresponding to the presence of the components contained in the eluent. Whether a component is contained in the test sample may be determined by examining the existence of the corresponding peak.

To obtain high purity, it is desirable that the peaks be well separated. To achieve high concentration, it is desirable that the peaks be narrow. To accurately determine whether a component is contained in the test sample, it is desirable that the response peaks in the plot are narrow and well separated. To obtain narrow or well-separated, well-defined response peaks, it is desirable that the flow of the fluid, such as the test sample and/or the eluent, through the separation medium is uniform. Uniform fluid flow through a separation medium may be characterized by such parameters as uniform flow rate per unit area across the entire flow area and uniform residence time for fluid traversing each streamline of the flow. Residence time is defined as the time during which a fluid particle

is within the chromatography device as a whole or within one or more parts of the chromatography device, such as the separation medium.

In many conventional chromatography devices, the flow of the test sample is non-uniform. For example, the test sample entering the separation medium may not be uniformly distributed across the entire flow area and "channeling" may occur as a result. "Channeling" is a phenomenon where certain areas of the fluid front of the test sample have a higher flow rate than other areas of the fluid front. The portions of the separation medium experiencing higher flow rates may encounter greater quantities of the components and may become saturated before other portions of the separation medium. This may cause the component to "break through" to the outlet of the device before the entire medium is saturated, thus reducing the total quantity of the component that may be captured before some is lost at the outlet.

The non-uniform flow of an eluent may cause a component to appear sooner in a portion of the eluent having a higher flow rate and later in a portion of the eluent having a lower flow rate. Even if the eluent has uniform flow rates, non-uniform residence times may cause the component to appear sooner in a portion of the eluent having a shorter residence time and later in a portion of the eluent having a longer residence time. These phenomena may cause the component to appear in the different streamlines of the eluent at different times. Consequently, non-uniform flow may cause the component to appear in a longer segment of the eluent flow stream at a lower concentration, making the response peaks wider and less concentrated. Wider and less concentrated response peaks may lead to an overlapping of the response peaks, making the identification of the response peaks, and consequently the identification and separation of the corresponding components, more difficult.

One source of non-uniform flow in conventional chromatography devices is frequently a non-uniform distribution of incoming and outgoing fluid. In a typical chromatography device, the incoming fluid passes from an inlet passage into a separation medium that generally has a much larger flow area than the inlet passage. And the outgoing fluid passes from the separation medium into the outlet passage that generally has a much smaller flow area than the separation medium. Such changes in flow areas may

cause non-uniform flow because they generate flow disturbances such as vortices or because fluid traveling along the longer radially outward paths takes a longer time to flow from one flow area to another larger (or smaller) flow area than fluid traveling along the centerline.

SUMMARY OF THE INVENTION

This invention provides effective, simple flow distributor arrangements that can uniformly distribute fluid flow between two different flow areas.

In accordance with one aspect of the invention, a flow distributor arrangement comprises a tapered space and a porous flow distributor and may be used for distributing fluid flow in a chromatography device along a flow path between a first passage having a first flow area and a second passage having a second flow area larger than the first flow area. The tapered space is disposed in the flow path between the first passage and the second passage and is substantially free of structures, such as flow directors. The porous flow distributor is disposed in the flow path and is positioned such that fluid flowing between the tapered space and the first passage passes through the porous flow distributor.

In accordance with another aspect of the invention, a flow distributor arrangement comprises a first porous flow distributor, a second porous flow distributor, and a tapered space and may be used for distributing fluid flow in a chromatography device along a flow path between a first passage having a first flow area and a second passage having a second flow area larger than the first flow area. The first flow distributor is arranged to distribute fluid from or to the first passage. The second porous flow distributor is arranged to distribute fluid to or from the second passage. The tapered space is fluidly coupled to the first and second porous flow distributors to direct at least a portion of the fluid between the first and second flow distributors.

In accordance with another aspect of the invention, a flow distributor arrangement comprises a tapered space and a porous flow distributor and may be used for distributing fluid flow in a chromatography device along a flow path between a first passage and a second passage, where one of the passages has a larger flow area that the other passage. The tapered space is disposed in the flow path between the first passage and the second

passage. Further, the tapered space includes a first tapered section and a second tapered section disposed outwardly of the first tapered section. The porous flow distributor is disposed in the flow path and fluidly coupled to the tapered space.

In accordance with another aspect of the invention, a flow distributor arrangement comprises a tapered space and a porous flow distributor and may be used for distributing fluid flow in a chromatography device along a flow path between a first passage having a first flow area and a second passage having a second flow area larger than the first flow area. The tapered space is disposed in the flow path between the first passage and the porous flow distributor. The porous flow distributor is disposed in the fluid flow path between the tapered space and the second passage.

In accordance with another aspect of the invention, a method for distributing fluid along a flow path in a chromatography device comprises directing the fluid along the flow path through a first passage having a first flow area, passing the fluid through a flow distributor arrangement disposed in the flow path and including a tapered space and a porous flow distributor fluidly coupled to one another, and directing the fluid along the flow path through a second passage having a second flow area different from the first flow area.

In accordance with another aspect of the invention, a chromatography device comprises an inlet, an outlet, a porous medium module, and a flow distributor arrangement. The porous medium module includes a stack of porous media disposed in a flow path between the inlet and the outlet. The porous media have a flow area larger than a flow area of at least one of the inlet and the outlet. The flow distributor arrangement is disposed in the flow path between the porous media and said one of the inlet and the outlet. The flow distributor arrangement includes a tapered space and a porous flow distributor fluidly coupled to the tapered space. The tapered space is disposed in the flow path between the porous media and said one of the inlet and the outlet and is substantially free of structures. The porous flow distributor is positioned such that fluid flowing between the tapered space and said one of the inlet and the outlet passes through the porous flow distributor.

In accordance with another aspect of the invention, a chromatography device comprises an inlet, an outlet, a porous medium module, and a flow distributor arrangement. The porous medium module includes a stack of porous media disposed in a flow path between the inlet and the outlet. The porous media have a flow area larger than a flow area of at least one of the inlet and the outlet. The flow distributor arrangement is disposed in the flow path between the porous media and said one of the inlet and the outlet. Further, the flow distributor arrangement includes a tapered space and a porous flow distributor fluidly coupled to the tapered space. The tapered space is disposed in the flow path between the porous media and said one of the inlet and the outlet. The porous flow distributor is disposed in the flow path between the tapered space and the porous media and is integrally secured to the porous medium module.

In accordance with another aspect of the invention, a chromatography device comprises an inlet, an outlet, a porous medium module, and a flow distributor arrangement. The porous medium module is disposed in a fluid flow path between the inlet and the outlet. The porous medium module includes a stack of porous media having a first end and a porous medium support supporting the first end of the stack of the porous media. The flow distributor arrangement is disposed in the flow path between the porous medium support and one of the inlet and the outlet. The flow distributor arrangement includes a tapered space and a porous flow distributor fluidly coupled to the tapered space.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a sectional view of one embodiment of a chromatography device.

Figure 2 is a sectional view of one embodiment of a flow distributor arrangement.

Figure 3 is a sectional view of another embodiment of a flow distributor arrangement.

Figure 4 is a sectional view of another embodiment of a flow distributor arrangement.

Figure 5 is a partial sectional view of another embodiment of a chromatography device.

Figure 6 is a plan view of the plate of the stationary medium holder of Figure 5.

Figure 7 is a plan view of another plate.

Figure 8 is an exploded sectional view of another chromatography device incorporating the plate of Figure 7.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Figure 1 illustrates one example of a chromatography device 10 embodying the invention. The exemplary chromatography device 10 may include first and second ports, e.g., an inlet 12 and an outlet 14, a stationary separation medium 22, a stationary medium holder 40 retaining the stationary separation medium 22, and first and second flow distributor arrangements 52, 54. The stationary medium holder 40 may define a flow path between the inlet 12 and the outlet 14, and the stationary separation medium 22 may be disposed in the flow path. The first flow distributor arrangement 52 may be disposed in the flow path between the inlet 12 and the stationary separation medium 22, and the second flow distributor arrangement 54 may be disposed in the flow path between the stationary separation medium 22 and the outlet 14. Alternatively, the first and second flow distributor arrangements may be operatively associated with and/or fluidly coupled to the outlet and inlet, respectively, or only a first or second flow distributor arrangement may be included in the chromatography device.

In the illustrated embodiment, the stationary separation medium comprises a stack of porous separation media, preferably a stack of porous membranes, although the stationary separation medium may be of any suitable type, such as a bed of particles, e.g., a bed of resin beads. Some preferred porous separation media are described in detail in United States Patent Application No. 60/121,668 by Chung-Jen Hou, Peter Konstantin and Yujing Yang, entitled “Negatively Charged Membrane” and filed February 25, 1999; an International Application by Chung-Jen Hou, Peter Konstantin and Yujing Yang, entitled "Negatively Charged Membrane" and filed February 25, 2000; United States Patent Application No. 60/121,669 by Jayesh Dharia, Chung-Jen Hou, Peter Konstantin and Yujing Yang, entitled “Positively Charged Membrane” and filed February 25, 1999; United States Patent Application No. 60/121,670 by Xiaosong Wu, Jayesh Dharia, Peter Konstantin and Yujing Yang, entitled “Positively Charged Membrane” and filed February

25, 1999; an International Application by Xiaosong Wu, Jayesh Dharia, Chung-Jen Hou, Peter Konstantin, and Yujing Yang, entitled "Positively Charged Membrane" and filed February 25, 2000; and United States Patent Application No. 60/134,197 by Xiaosong Wu, Joe Kinsey, and Michael Ishee, entitled "Endotoxin Retentive Membranes" and filed May 14, 1999. These patent applications are incorporated by reference in their entirety.

The stack of porous media 22 may be arranged in a variety of configurations. For example, the stacked porous media may be disposed and sealed at any suitable location in the chromatography device 10. The stacked porous media may be sealingly disposed in a porous medium module holder having a hollow, cylindrical configuration. In the embodiment shown in Figure 1, the stationary separation medium comprises the stacked porous media 22 disposed in a porous medium module 20. The porous medium module 20 may include a hollow support member 26 containing the stacked porous media 22, and a sealant 24 disposed between the support member 26 and the stacked porous media 22. The sealant 24 prevents fluid that passes axially through the porous media 22 from leaking radially out of the porous media 22. In a preferred embodiment, the sealant 24 may penetrate into the outer periphery of the stacked porous media 22 to form a strong, effective seal and/or bond.

In some embodiments, the porous medium module 20 may also include first and/or second porous medium supports 30, 32 disposed respectively at the ends of the stack of porous media 22. As shown in Figure 1, the first and second porous medium supports 30, 32 are each integrally secured to the porous medium module 20, for example, by the sealant 24. Alternatively or additionally, the porous medium module may include one or more porous medium supports within the stacked porous media.

The first and second porous medium supports 30, 32 may perform any one or more of a number of functions. For example, the porous medium supports 30, 32 may support and protect the axial ends of the stack of porous media 22. They may be used to provide uniform axial compression to the stack of porous media 22 to prevent the porous media 22 from, for example, bulging at the center of the porous media 22, and thereby providing a uniformly packed porous media 22.

The porous medium supports 30, 32 may have any suitable structure that allows the porous medium supports to perform one or more of the above functions. Each porous medium support may be a single layer structure or a multilayer structure. The porous medium supports may be fashioned from a wide variety of materials and configurations. Materials suitable for the porous medium supports include metals, ceramics, and polymers. Configurations suitable for the porous medium supports include perforated plates and rigid screens or meshes, which may have openings sized from about 25 microns or less to about 0.62 inch or more, preferably from about 0.010 inch to about 0.030 inch. The porous medium supports may also include a rigid porous sheet, supported or unsupported, of bonded or sintered metallic or polymeric particles or fibers having finer openings, e.g., a 0.08 inch thick unsupported sheet of sintered stainless steel particles.

Some preferred porous medium modules are described in detail in United States Patent Application No. 60/121,667 by Mark Hurwitz, Thomas Fendya, and Gary Bush, titled "Chromatography Devices, Porous Medium Modules Used in Chromatography Devices, and Methods for Making Porous Medium Modules" and filed on February 25, 1999; United States Patent Application No. 60/168,738 by Mark Hurwitz, Thomas Fendya, Thomas Sorensen, John Strempel, and Gary Bush, titled "Chromatography Devices, Porous Medium Modules Used in Chromatography Modules, and Methods for Making Porous Medium Modules" and filed December 6, 1999; and an International Application by Mark Hurwitz, Thomas Fendya, Thomas Sorensen, John Strempel, and Gary Bush, titled "Chromatography Devices, Porous Medium Modules Used in Chromatography Modules, and Methods for Making Porous Medium Modules" and filed February 25, 2000, which applications are incorporated in their entirety by reference.

A variety of stationary medium holders may be used in the chromatography device 10. For example, in the embodiment shown in Figure 1, the stationary medium holder comprises a porous medium module holder 40 which preferably includes two holder sections such as opposed plates 42, 44 between which the porous medium module 20 may be disposed. Connectors, such as a plurality of bolts 46 or clamps, may secure the porous medium module 20 between the two plates 42, 44. In the illustrated embodiment, the inlet 12 and outlet 14 are preferably placed near the center of the two plates 42, 44,

respectively. Each of the inlet 12 and outlet 14 may include a female threaded socket intended to receive a male threaded fitting with substantially the same inner diameter as the passage 16, 18. A first flow distributor arrangement 52 may be disposed concentrically in the flow path between the inlet 12 and the porous media 22 (or the porous medium module 20) and/or a second flow distributor arrangement 54 may be disposed concentrically in the flow path between the porous media 22 (or the porous medium module 20) and the outlet 14.

Alternatively, the porous medium module holder may have any suitable configuration. For example, the porous medium module holder may have a hollow, cylindrical configuration or a configuration similar to that of a container. The inlet and outlet may be placed at any suitable location, as long as they allow a fluid, such as a test sample or an eluent, to enter and exit the chromatography device, respectively. Alternatively, the porous medium holder may have a plurality of inlets and a plurality of outlets to more uniformly distribute the fluid, especially for porous media having large diameters. In some embodiments, the porous medium module holder may include a key mechanism that ensures that the porous medium module holder and the porous medium module are properly aligned when the porous medium module is disposed in the porous medium module holder.

Seals 48, 49 may be provided to prevent fluid from leaking through the gaps between the porous medium module 20 and the plates 42, 44 of the porous medium module holder 40. The seals 48, 49 may be of any suitable type and may be integral or unitary with the sealant 24 of the porous medium module 20. For example, the seals may be ring seals or annular gaskets. The plates 42, 44 or the porous medium module 20, or both, may have an annular groove to accommodate each of the seals 48, 49. When each of the seals is compressed into an annular groove, the seal preferably seals the opening of the groove from the fluid so that the fluid will not flow into the groove, preventing the formation of stagnant flow areas in the groove.

In the embodiment shown in Figure 1, the seals 48, 49 are ring seals having a generally rectangular (or trapezoidal) cross-section, and the grooves have a generally trapezoidal (or rectangular) cross-section. The seals and grooves are so dimensioned that,

when the seals are compressed into the grooves, the openings of the grooves are substantially sealed by the seals from the fluid. In the illustrated embodiment, the inner diameters of the seals 48, 49 preferably are substantially the same as the diameter of the axial flow area in the stacked porous media 22. This prevents the formation of stagnant regions in the gaps between the porous medium module 20 and the plates 42, 44. Fluid flowing into and out of any stagnant regions may create non-uniform flow rates and residence times.

The embodiment shown in Figure 1 preferably includes both first and second flow distributor arrangements 52, 54. The flow path through the inlet passage 16 has a smaller flow area than the flow path at the porous media 22, and the first flow distributor arrangement 52 preferably is disposed in the flow path between the inlet passage 16 and the stacked porous media 22. The flow path at the porous media 22 has a larger flow area than the flow path through the outlet passage 18, and the second flow distributor arrangement 54 preferably is disposed in the flow path between the stacked porous media 22 and the outlet passage 18. Generally, a flow distributor may be disposed at any place in the flow path, for example, where there is a change in flow areas.

As shown in Figure 2, the first flow distributor arrangement 52 preferably includes a tapered space 60 and a porous flow distributor 56 that is operatively associated with the tapered space 60. The tapered space 60 comprises at least a portion of the transition in the flow path between the smaller area inlet passage 16 and the larger area porous media 22. The tapered space may be any arrangement that allows the fluid flowing from the inlet passage 16 to the porous media 22 to have a substantially more uniform residence time. The tapered space may also be any arrangement that produces a substantially more uniform axial flow rate for all flow streamlines at the face of the stationary separation medium, e.g., the face of the porous medium module. Further, the tapered space may be any arrangement that produces a substantially uniform fluid flow, for example, by enhancing the uniformity of the residence time and/or the axial flow rate at the face of the porous medium module. The tapered space may accomplish any of the above functions either alone or in combination with one or more other components of the flow distributor arrangement.

The tapered space may have any suitable configuration. In the embodiment shown in Figure 2, the tapered space 60 has a substantially conical configuration that has a straight tapered end and a flat end, although a tapered space may have any other suitable configuration that has a curved tapered end, such as a hyperbolic, quadratic, cubic or semispherical tapered end. Generally, the tapered space may have any regular or irregular configuration that is thicker at the inlet (or outlet) location(s) and thinner at the outer periphery, including, for example, a configuration that has two straight or curved tapered ends.

The configuration of the tapered space or a segment thereof may be selected so that the flow area of the tapered space has various desirable characteristics. For example, the configuration of the tapered space may be selected so that the flow area for radially outward flow remains constant or increases (or decreases) with the radius of the tapered space.

The configuration of the tapered space or a segment thereof may also be selected so that the fluid flow within the tapered space may have various desirable characteristics. For example, the configuration of the tapered space may be such that the fluid flowing through the tapered space has substantially uniform residence time. To achieve a substantially uniform residence time, the fluid traveling along the radially outward paths preferably has a high radial flow rate. In determining the configuration of the tapered space for achieving desired radial flow rates, the permeability of the stationary separation medium, e.g., the porous medium module, including the permeability of the porous medium support and/or the porous media, preferably may also be considered. One reason for considering the permeability of the porous medium module may be that the radial flow rates at a given radius are determined by both the flow area at the radius and the flow volume at the radius. While the flow may be determined by the configuration of the tapered space, the flow volume may be determined, in part, by the permeability of the porous medium module. The more permeable the porous medium module may be, the less the fluid volume may be at a given radius because more fluid has exited the tapered space and entered the porous medium module before the fluid reaches the radius.

The tapered space 60 may be formed in any suitable way. In the illustrated embodiment, the tapered space 60 is formed by a tapered recess or projection located solely in a plate 42 of the porous medium module holder 40. Alternatively, the tapered space may be formed by a tapered recess or projection located solely in the porous medium module, e.g., in the porous medium support. Further, the tapered space may be formed by a combination of a recess or projection in the plate and a recess or projection in the porous medium module. In some embodiments, the tapered space may be formed, in part or in whole, by a part disposed between the plate and the porous medium module.

As shown in Figure 2, the tapered space 60 of the first flow distributor arrangement 52 may be substantially free of any structures, including support structures, such as protrusions, and structures, such as ribs or walls, which define flow passages. In conventional flow distribution arrangements, a substantial number of protrusions are often provided to support the porous media and prevent the porous media from protruding into the flow space, and a substantial number of ribs or walls defining flow passages are often provided to guide fluid flow in the flow space.

As shown in Figures 1 and 2, the tapered space 50 is preferably substantially free of structures because they may cause non-uniform flow and/or flow disturbances. Protrusions may disrupt fluid flow and cause flow disturbances, and ribs or walls defining flow passages may cause non-uniform flow because the fluid near the ribs or walls has lower velocities than the fluid in the middle of the flow passages.

A tapered space that is substantially free of structures may be completely free of any structures or may nonetheless have a small number of structures where those structures do not cause any substantial non-uniform flow or flow disturbances. For example, the tapered space may have a small number of support structures, e.g., about four to about eight angularly-spaced studs having an elongated, fairing, or foil shape, that are arranged to minimize non-uniform flow and flow disturbances. These structures may be arranged to support the porous media and/or the porous medium supports and to prevent the porous media from protruding into the tapered space and interfering with the fluid flow in the tapered space. Although the tapered space in the embodiment shown in Figures 1 and 2 does not include any structures, the tapered spaces in other embodiments,

e.g., embodiments where the diameter of the porous media is about 10.0 cm or more, may include a small number of structures to support the porous media and/or the porous medium supports.

The porous flow distributor may be any porous structure that reduces flow disturbances, such as flow recirculations, vortices, and eddies, within the tapered space. Alternatively or additionally, the flow distributor may be any porous structure that enhances the uniformity of flow characteristics, such as flow rates and residence times.

The porous flow distributor may be formed from a variety of materials, such as a metallic, polymeric or ceramic material compatible with the test samples and eluents. Preferred materials include bonded or sintered metallic or polymeric particles, or sintered glass beads. For example, the flow distributor may be formed from a sintered metal powder, such as a sintered stainless steel powder. An example of sintered or bonded polymeric particles comprises polymeric beads that are sintered or bonded with heat or with a solvent or adhesive. The polymeric beads may be formed from any suitable polymeric material, such as polyethylene, polypropylene, polysulfone, teflon, polyethersulfone or polytetrafluoroethylene. Alternatively, the flow distributor may be formed from a natural, synthetic or metallic fibrous material.

In the embodiment illustrated in Figure 2, the flow distributor 56 preferably comprises a porous structure that reduces flow disturbances and non-uniformities as the fluid enters the tapered space 50 from the inlet passage 16. The flow distributor 56 preferably is placed in the flow path and fluidly coupled to the tapered space, wherein the fluid which flows from the inlet passage to the tapered space passes through the porous flow distributor. For example, the porous flow distributor 56 is preferably mounted to the inner plate 44, and an end of the porous flow distributor 56 preferably extends into the plate 44 at the inlet passage 16, although in other embodiments, the end may only abut the plate 44 without extending into it. The other end of the porous flow distributor 56 may be spaced from, may abut, or may extend into the porous medium module, e.g., the porous medium support 30.

The porous flow distributor of the first flow distributor arrangement 52 may be variously configured. In the illustrated embodiment, the porous flow distributor 56 has a

generally cylindrical configuration with a uniform thickness, although the porous flow distributor may have any suitable configuration with a varied thickness, such as a conical, semispherical, parabolic, trapezoidal configuration. For example, if when the fluid reaches the flow distributor, the flow rates are, for example, greater near the center of the flow distributor than they are around the outer periphery, the flow distributor may be made thicker (or less permeable) at the center to provide more flow resistance to the flow at the center, and thinner (or more permeable) near the outer periphery to provide less flow resistance to the flow near the outer periphery. Thus, when the fluid exits the flow distributor, it may have a more uniform flow rate.

The cylindrical porous flow distributor 56 may have any suitable height and/or diameter. For example, the height of the porous flow distributor 56 may be less than that of the tapered space 60 at the center. Alternatively, the height of the porous flow distributor 56 may be substantially the same as or greater than the height of the tapered space 60 at the center. The diameter of the porous flow distributor 56 may be substantially the same as that of the inlet passage 16. Alternatively, the diameter of the porous flow distributor 56 may be greater than that of the inlet passage 16. In some embodiments, the diameter of the porous flow distributor 56 may be in the same range as that of the tapered space 60.

Preferably, the permeability of the flow distributor 56 is substantially uniform such that the distributor 56 has substantially uniform radial and/or axial flow characteristics. Thus, if the flow distributor 56 is formed from sintered or bonded particles, the particle sizes preferably are substantially uniform because the uniformity of distributor permeability may be closely related to the uniformity of the particle size. Additionally, at least two factors are preferably considered in selecting the permeability of the flow distributor 56. First, the permeability of the flow distributor 56 preferably is small enough to dampen or prevent any substantial flow disturbances near the intersection of the inlet passage 16 and the tapered space 60 or non-uniform flow characteristics within the tapered space 60. Second, the permeability preferably is large enough to avoid any substantial pressure drop through the flow distributor 56 or substantial slowing of the flow in the radial direction.

Alternatively, the flow distributor may have various non-homogenous characteristics which retard flow disturbances and/or non-uniform flow characteristics. For example, the flow distributor may have a varying permeability, which may vary axially and/or radially, continually or in a stepwise manner. The flow distributor may also comprise multiple sections, which may have similar or different characteristics.

The first flow distributor arrangement may include one or more additional components. For example, in addition to or as an alternative to the flow distributor 56 shown in Figures 1 and 2, the flow distributor arrangement may include one or more flow distributors placed anywhere upstream or downstream of the tapered space or within the tapered space. For example, the first flow distributor arrangement may include, in addition to the first porous flow distributor 56, a second porous flow distributor which may be similar to the first porous flow distributor and may be disposed between the tapered space and the stationary separation medium. For example, the second porous flow distributor, like the first porous flow distributor, may be any porous structure that reduces flow disturbances and/or provides more uniform flow characteristics for fluid flowing between the tapered space and the stationary separation medium.

The second flow distributor may be located in the plate 44 of the porous medium module holder or, preferably, it may be located in the porous medium module. In the embodiment shown in Figure 2, the second flow distributor preferably comprises the porous medium support 30 of the porous medium module and is therefore integrally secured to the porous medium module. The second porous flow distributor then serves not only to reduce or retard flow disturbances and/or flow non-uniformities but also to support the porous media within the porous medium module.

In many preferred embodiments, the first flow distributor arrangement may not include a flow distributor between the inlet passage and the tapered space, e.g., may not include the first flow distributor 56. For example, as shown in Figure 3, the first flow distributor arrangement 52 may include a tapered space 60 and only a single flow distributor, e.g., the second flow distributor which serves as the porous medium support 30 and is disposed between the tapered space 60 and the stationary separation medium 22. In other preferred embodiments, the first flow distributor arrangement may generally

include both the flow distributor between the inlet passage and the tapered space and the flow distributor between the tapered space and the stationary separation medium. The flow distributor between the tapered space and the stationary separation medium may be structurally similar to or different from the flow distributor between the inlet passage and the tapered space.

The description of the various components, configurations, and functions of the first flow distributor arrangement 52 are substantially applicable to the second flow distributor arrangement 54, except the second flow distributor arrangement 54 is disposed in the flow path between the stationary separation medium 22 and the outlet 14. If a symmetrical chromatography device is desired, the first and second flow distributor arrangements 52, 54 preferably are structurally similar and are similarly arranged respectively between the inlet passage 16 and the porous media 22 and between the outlet passage 18 and the porous media 22. Alternatively, the second flow distributor arrangement may be structurally different from the first flow distributor arrangement, and it may have any of the alternative embodiments described in the discussion of the first flow distributor arrangement. For example, as shown in Figure 4, the second flow distributor arrangement 54' may include a tapered space 62 and only a single flow distributor, such as a conically-shaped porous medium support 32', between the porous media 22 and the tapered space 62.

In the specific example of an embodiment of a chromatography device 10 shown in Figures 1 and 2, the first and second flow distributor arrangements 52, 54 are substantially similar. Each includes first and second porous flow distributors 56, 30, 58, 32 comprising a sintered mass of stainless steel powder having, for example, a nominal particle size on the order of about 50μ. The first flow distributor 56, 58 may each comprises a porous disk having an outer diameter of about 6 mm, an uniform thickness of about 2 mm, and a uniform porosity wherein the nominal pore size is on the order of about 25μ. The tapered space 60, 62 may have an outer diameter of about 31 mm, which is about the same as the diameter of the effective flow path through the porous medium module 20, and a straight conical taper with a gap thickness about 0.8 mm at the outer

edge of the first flow distributor 56, 58 and a small gap at the seal 48, 49, e.g., about a few thousandths of an inch.

A preferred mode of operation of a chromatography device of the present invention may be illustrated while referring to the embodiment shown in Figure 1. The fluid flow characteristics may vary depending on, for example, the nature of the separation, the test sample, and/or the eluent. For example, in a preferred embodiment, the fluid may be passed through the chromatography device 10 at a system pressure of about 200 psi, a pressure differential across the porous medium module of about 100 psid, and a flow velocity in the range from about 1 cm/min to about 10 cm/min. At a given flow velocity, the flow rate of the chromatography device varies with the effective flow area of the device.

A fluid, such as a test sample or an eluent, may be introduced into the chromatography device 10 along a fluid flow path through the inlet passage 16. From the inlet passage 16, the fluid passes through the first flow distributor arrangement 52 disposed in the fluid flow path into the stationary separation medium 22, the flow area of the passage through the stationary separation medium 22 being different, i.e., larger than, the flow area of the inlet passage. For example, in the illustrated embodiment the fluid passes from the inlet passage 16 through the first porous flow distributor 56 and into the tapered space 60. The flow distributor 56 may reduce flow disturbances, such as flow recirculations, vortices, and eddies, and flow non-uniformities as the fluid flows into the tapered space 60 from the inlet passage 16.

The tapered space 60 preferably distributes uniformly the fluid from the inlet passage 16 to the porous medium module 20, which has a larger flow area than the inlet passage 16. In the illustrated embodiment, the tapered space 60 enhances the distribution of the fluid from the inlet passage 16 to the second porous flow distributor, e.g., the porous medium support 30 of the porous medium module 20. For example, the tapered space 60, especially a tapered space substantially free of structures, may provide a more uniform residence time and/or axial flow rate at the face of the porous medium module 20. From the tapered space 60, the fluid flows through the second flow distributor 30. The second flow distributor further reduces flow disturbances and enhances the uniformity of

flow rates and residence times as the fluid flows from the tapered space 60 into the stationary separation medium 22.

After passing through the stationary separation medium 22, the fluid passes through the second flow distributor arrangement 54 disposed in the flow path to the outlet passage 18, the flow area of the outlet passage 18 being different from, i.e., smaller than, the flow area of the passage through the stationary separation medium 22. For example, in the illustrated embodiment, the fluid passes through the second porous flow distributor, e.g., the porous medium support 32, through the tapered space 62 through the first porous flow distributor 58 to the outlet passage 18. Each of the components of the second flow distributor arrangement 54 functions in a manner analogous to the components of the first flow distributor arrangement 52 to provide more uniform flow characteristics for fluid flowing to the outlet passage 18. For example, the second flow distributor, e.g., the porous medium support 32, may reduce flow disturbances and enhance the uniformity of the flow rates and residence times as the fluid flows from the stationary separation medium 22 into the tapered space 62. The tapered space 62, especially a tapered space substantially free of structures, may provide more uniform residence times and axial flow rates. The first porous flow distributor 58 may reduce flow disturbances as the fluid flows from the tapered space 62 into the outlet passage 18.

By providing more uniform flow characteristics into and/or out of the stationary separation medium, the first and/or second flow distributor arrangements significantly enhance the chromatographic separations of the stationary separation medium. For example, the chromatographic resonance peaks may be much more narrow, well-separated and well-defined that those resulting from conventional chromatographic separations.

Once the chromatographic separation has been completed, the porous medium module 20 may be cleaned or replaced in preparation for the next separation. For example, the connectors 46 may be loosened or removed, and the used porous medium module 20 may be removed from between the plates 42, 44 of the porous medium module holder 40. The porous medium module 20, including each integrally secured flow distributor 30, 32, may then be thoroughly cleaned, removing all residue of the previous chromatographic separation from both the flow distributors 30, 32 and the stationary

separation medium, e.g., the stack of porous media 22. The plates 42, 44 may also be thoroughly cleaned. The cleaned porous medium module 20, or a new or previously cleaned porous medium module 20, may then be inserted between the clean plates 42, 44 along with new or cleaned seals 48, 49 and secured in place. Another chromatographic separation may then proceed.

By providing a chromatographic device in which at least one of the flow distributors, and preferably the sole flow distributor, of each flow distributor arrangement is integrally secured to the porous medium module, the chromatographic separations are even further enhanced. Removal of each flow distributor 30, 32 along with the porous medium module 20 allows full access to both the flow distributors 30, 32 and the taper spaces 60, 62 to ensure they are thoroughly cleaned of any residue from previous chromatographic separations, thereby avoiding contamination of subsequent separations.

Another specific example of an embodiment of a chromatographic device 100 is shown in Figures 5 and 6. As shown in Figure 5, the second chromatography device 100 includes a stationary separation medium 122 and a stationary medium holder 140. Preferably, the stationary separation medium comprises stacked porous membrane media 122 disposed in a porous medium module 120 which further includes a hollow support member 126, a sealant 124 and first and second porous medium supports 130. The stationary medium holder 140 includes two plates 144 between which the porous medium module 120 may be disposed and held in place by any suitable connector. A first flow distributor arrangement 152 may be disposed in the flow path between an inlet 112 and the porous media 122. A second flow distributor arrangement, which is preferably substantially similar to the first flow distributor arrangement 152, may be disposed in the flow path between the porous media 122 and an outlet. Each of these components is analogous to those of the chromatography device 10 shown in Figures 1 and 2.

The flow distributor arrangements of the second chromatography device 100 have many features in common with the flow distributor arrangements shown in Figures 1 and 2. For example, the first flow distributor arrangement 152 shown in Figure 3 includes a tapered space 160 and a second flow distributor, e.g., the first porous media support 130. The second flow distributor 130 is preferably integrally secured to the porous medium

module 120, e.g., by the sealant 124. Further, the second flow distributor may comprise a porous disk having an outer diameter of about 45 mm, which is about 6 mm greater than the diameter of the porous media 122, a uniform thickness of about 2 mm to 4 mm and a uniform porosity wherein the nominal pore size is on the order of about 25μ. However, the first flow distributor arrangement 152 preferably does not have a first flow distributor interfacing between the inlet passage 116 and the tapered space 160. The second flow distributor 130 disposed between the tapered space 160 and the porous media 122 is the sole porous flow distributor of the first flow distributor arrangement 152. Similarly the second flow distributor arrangement preferably does not have a first flow distributor, having only a single porous flow distributor integrally secured to the porous medium module 120 and located between the stationary porous media 122 and the tapered space. The flow distributor of the second flow distributor arrangement is preferably substantially similar to the flow distributor of the first flow distributor arrangement. Alternatively, they may have different characteristics, e.g., different configurations and/or permeabilities.

The tapered space of each flow distributor arrangement of the second chromatography device 100 differs from the tapered space of the flow distributor arrangements of the first chromatography device 10. For example, the tapered space 160 of the second chromatography device 100 may be larger, e.g., having an outer diameter of about 39 mm, which is about the same as the diameter of the effective flow path through the porous medium module 120, and may have a generally conical taper with a gap thickness, for example, of about 1 mm at the inlet passage 116 and a gap that is small at the seal 148, 149, e.g., about a few thousandths of an inch.

Further, while the tapered spaces of both devices 10, 100 are substantially free of structures, the tapered space 160 of the second chromatography device 100 preferably includes a plurality of elongated support studs 161, e.g., six studs 161 equally angularly spaced within the tapered space 160, as shown in Figure 4. The studs 161 may extend axially from the plate 144 toward the porous medium module 120 and extend radially preferably less than about 33%, more preferably less about 25% or less than about 20%, of the radius of the tapered space 160. The studs 161 function to support the porous flow

distributor 130 and/or the porous medium module 120 including the porous medium supports 130 over the tapered space 160. The studs 161 may be machined on a flat 162 in the tapered space 160. The flat 162 preferably extends in a plane generally perpendicular to the axis of the chromatography device 100 and divides the tapered space 160 into two tapered sections 163, 164 spaced from each other. The inner tapered section 163 preferably extends from near the inlet passage 116 towards the outer seal 149, while the outer tapered section 164 preferably extends from near the outer seal 149 towards the inlet passage 116. Each tapered section preferably has a straight conical taper, and the taper of the inner tapered section 163 is preferably steeper than the taper of the outer tapered section 164.

In the illustrated embodiment, the studs 161 extend from the plate 144 toward the porous flow distributor 130 and the porous medium module 120. Alternatively, the studs may extend from the porous flow distributor or the porous medium module toward the plate. Preferably, a stud extends toward a flat section of the plate, although it may extend toward any part of the plate, e.g., a tapered section of the plate. Thus, if the studs extend from the porous flow distributor and/or porous medium support, the plate may be formed with a continuous taper free of flats. Each stud may form a unitary or integral part of the porous flow distributor/porous medium support and preferably is made of the same material as the porous medium support, i.e., a porous material. Porous studs are advantageous because they weigh less and are less disruptive to the fluid flow. Alternatively, the studs may be a part separate from the porous medium module and the plate and may be disposed between the porous medium module and the plate. In general, any suitable structure, which does not cause any substantial non-uniform flow or flow disturbances, may be provided to support a porous medium support and prevent the porous medium support from protruding into a tapered space.

While the tapered space 160 of the illustrated chromatography device 100 has two spaced tapered sections 163, 164, each having straight conical tapers but different slopes, the tapered space may be configured in a wide variety of different ways to reduce flow disturbances and enhance uniform flow characteristics. For example, the tapered space may include more than two tapered sections, or each tapered section may have a curved

taper, or the tapered sections may have substantially similar slopes. Further, while the tapered sections 163, 164 of the illustrated device 100 are separated by a flat 162, the spaced tapered sections may be contiguous. The support studs may then extend from tapered wall of the plate 144 of either or both tapered sections. Alternatively, the support studs may extend from the porous medium support into the tapered space.

An example of another plate having a tapered space including tapered sections is shown in Figure 7. This plate 170 is analogous to the plate 144 shown in Figure 6 but may be much larger. The plate 170 shown in Figure 7 has a tapered space 171 including five tapered sections 172-176. The first tapered section 172, e.g., the inner tapered section, communicates with the inlet passage 116, and the fifth tapered section 176 comprises the outer tapered section. The configuration of the tapered sections 172-176 may be similar to the configuration of the tapered sections 163, 164 shown in Figure 6. One or more of the tapered sections may have a 0° taper, i.e., may be substantially flat, but it is preferred that each of the tapered sections have a taper greater than 0°, although the tapers may differ from the one tapered section to another.

In the embodiment shown in Figure 7, the five tapered sections 172-176 are preferably separated by four flats 180-183 and each flat 180-183 includes a plurality of support studs 184. The support studs 184 may be similar to the studs 161 shown in Figure 6 and serve to support a porous flow distributor and/or a porous medium module over the tapered space 171. A porous flow distributor spanning the tapered space 171 preferably has a tapered surface facing the tapered space 171. Consequently, the height or axial position of the faces of the studs 184 may vary from one flat to another in correspondence with the tapered face of the flow distributor.

A preferred mode of operation of the second chromatography device 100 shown in Figure 5, including cleaning and/or replacing the porous medium modules 140 and plates 144, is analogous to the previously described preferred mode of operation of the first chromatography device 10. However, as the fluid enters the tapered space 160 from the inlet passage 116 (or exists the tapered space through the outlet passage) of the second chromatography device 100, the fluid does not pass through a porous flow distributor. Rather, the fluid enters (or exits) the inner tapered section 163 of the tapered space 160

directly. Further, as the fluid flows through the tapered space, it passes the support studs 161 and enters (or exits) the outer tapered section 164. Preferably, the support studs 161 have a shape, e.g., a thin elongated shape with rounded leading edges, which resists the formation of flow disturbances and does not substantially increase the resistance to flow radially outwardly.

Another example of a chromatography device 200 is shown in Figure 8. In the illustrated embodiment, the chromatography device 200 includes the plate 170 shown in Figure 7, a flow distributor arrangement 201 including a tapered space 171 and a porous flow distributor 202, and a porous medium module 210. Each of these components may be analogous to the corresponding components of the previous embodiments. For example, the tapered space 171 may include several tapered sections 172-176, the inner tapered section 172 communicating with the inlet passage 116. The tapered sections 172-176 may be separated by flats 180-183 which include supporting studs 184. The porous flow distributor 202 preferably has a flat surface facing the porous medium module 210 and a tapered surface facing the tapered space 171. The taper of the porous flow distributor may have any suitable value. For example, the illustrated porous flow distributor 202 may have a diameter of about 15 inches and a straight conical taper defined by a thickness at the center of about 0.26 inch and a thickness at the outer peripheral region of about 0.17 inch. The porous medium module 210 preferably comprises a stack of porous media 211, a sealant 212 disposed around the outer periphery of the porous media stack, a hollow housing member 213, and a seal 214, all as previously described.

However, in the chromatography device 200 shown in Figure 8, the porous medium module 210 preferably includes a porous medium support 215 separate from the porous flow distributor 201. The porous medium support 215 is preferably integrally connected to the porous medium module 210, e.g., by the sealant 212, and may be fashioned from a screen or mesh, as previously described. The porous medium support 215 preferably has sufficient structural rigidity to support the compressed stack of porous media 211 but may be coarser, e.g., have larger openings, than the porous flow distributor 201.

The operation of the chromatography device 200 is similar to the operation of the previously described embodiments. The porous flow distributor 201 may be disposed in a fluid flow path through the chromatography device between the tapered space 170 and the porous medium support 215. Fluid flowing in either direction between the porous medium module 210 and the tapered space 170 flows through the porous flow distributor 201, and the porous flow distributor 201 serves to enhance flow uniformity as previously described. The porous flow distributor 201 may be mounted and sealed to the plate 170 and/or the porous medium module 210 in any suitable manner to prevent bypass of the fluid. The tapered surface of the porous flow distributor 201 may bear against the studs 184, while the flat surface of the porous flow distributor 201 may bear against the porous medium support 215. The porous flow distributor 201 is preferably removably mounted between both the plate 170 and the porous medium module 210. Disassembly of the plate 170, the porous flow distributor 201, and the porous medium module 210 greatly facilitates cleaning of these components.

While various aspects of the invention have been described with respect to several embodiments, many variations in these embodiments would be obvious to those of ordinary skill in the art in light of the teachings in this specification. For example, in accordance with the present invention, one or more or all of the features of any of the disclosed embodiments may be substituted and/or combined with one or more or all of the features of any of the other disclosed embodiments. For example, the first porous flow distributor 56 of the first flow distributor arrangement 52 of the first chromatography device 10 may be inserted between the inlet passage 116 and the tapered space 160 of the second chromatography device 100. Alternatively or additionally, the support studs 164 of the second chromatography device 100 may be included in one or both of the tapered spaces 60, 62 of the first chromatography device 10. Further, in accordance with the present invention, fewer than all of the features of each of the disclosed embodiments may be included. For example, the first flow distributor 58 of the second flow distributor arrangement 54 of the first chromatography device 10 may be eliminated. Alternatively, the flat 162 and the two tapered sections 163, 164 in the tapered space 160 of the second chromatography device 100 may be eliminated and the studs may extend from a plate wall

having a single conical taper which extends from near the inlet passage 116 to near the seal 149. Accordingly, all features, modifications and variations of the disclosed embodiments are encompassed within the spirit and scope of the invention as currently or hereafter claimed.

CLAIMS

1. A flow distributor arrangement for distributing fluid flow in a chromatography device along a flow path between a first passage having a first flow area and a second passage having a second flow area larger than the first flow area, the flow distributor arrangement comprising:

a tapered space in the flow path between the first passage and the second passage, the tapered space being substantially free of any structures; and

a porous flow distributor disposed in the flow path and fluidly coupled to the tapered space wherein fluid flowing between the tapered space and the first passage passes through the porous flow distributor.

2. The flow distributor arrangement according to claim 1, wherein the tapered space has an outer periphery, and the tapered space is thicker at a location adjacent to the first passage and thinner at the outer periphery.

3. The flow distributor arrangement according to claim 1 or 2, wherein the tapered space has a tapered end and a flat end.

4. The flow distributor arrangement according to claim 3, wherein the tapered end of the tapered space has a straight taper.

5. The flow distributor arrangement according to claim 3, wherein the tapered end of the tapered space has a curved taper.

6. The flow distributor arrangement according to any one of the preceding claims, wherein the tapered space is free of structures.

7. The flow distributor arrangement according to any one of the preceding claims, wherein the flow distributor is arranged to reduce flow disturbances as fluid enters or exits

the tapered space.

8. The flow distributor arrangement according to any one of the preceding claims including another fluid distributor disposed in the flow path between the tapered space and the second passage.

9. A flow distributor arrangement for distributing fluid flow in a chromatography device along a flow path between a first passage having a first flow area and a second passage having a second flow area larger than the first flow area, the flow distributor arrangement comprising:

a first porous flow distributor arranged to distribute fluid from or to the first passage;

a second porous flow distributor arranged to distribute fluid to or from the second passage; and

a tapered space fluidly coupled to the first and second porous flow distributors to direct at least a portion of the fluid between the first and second flow distributors.

10. The flow distributor arrangement according to claim 9, wherein the tapered space has an outer periphery, and the tapered space is thicker at a location adjacent to the first passage and thinner at the outer periphery.

11. The flow distributor arrangement according to claim 9 or 10, wherein the tapered space has a tapered end and a flat end.

12. The flow distributor arrangement according to claim 11, wherein the tapered end of the tapered space has a straight taper.

13. The flow distributor arrangement according to claim 11, wherein the tapered end of the tapered space has a curved taper.

14. The flow distributor arrangement according to any one of claims 9 to 13, wherein the tapered space is substantially free of structures.

15. The flow distributor arrangement according to any one of claims 9 to 14, wherein the first flow distributor is capable of reducing flow disturbances as fluid enters or exits the tapered space.

16. A chromatography device comprising:

an inlet and an outlet;

a porous medium module including a stack of porous media disposed in a flow path between the inlet and the outlet, the porous media having a flow area larger than a flow area of at least one of the inlet and the outlet; and

a flow distributor arrangement disposed in the flow path between the porous media and said one of the inlet and the outlet, the flow distributor arrangement including a tapered space and a porous flow distributor the tapered space being disposed in the flow path between the porous media and said one of the inlet and the outlet and being substantially free of structures, and the porous flow distributor is fluidly coupled to the tapered space wherein fluid flowing between the tapered space and said one of the inlet and the outlet passes through the porous flow distributor.

17. The chromatography device according to claim 16, wherein the tapered space has an outer periphery, and the tapered space is thicker at a location adjacent to the inlet and thinner at the outer periphery.

18. The chromatography device according to claim 16 or 17, wherein the tapered space has a tapered end and a flat end.

19. The chromatography device according to claim 18, wherein the tapered end of the tapered space has a straight taper.

20. The chromatography device according to claim 19, wherein the tapered end of the tapered space has a curved taper.

21. The chromatography device according to any one of claims 16 to 20, wherein the tapered space is substantially free of structures.

22. The chromatography device according to any one of claims 16 to 21 including a stationary separation medium holder including first and second plates, the first plate including the inlet and the second plate including the outlet, the porous medium module being disposed between the first and second plates.

23. The chromatography device according to claim 22, wherein the tapered space includes a recess in the first plate.

24. The chromatography device according to claim 22 or 23, wherein the porous flow distributor is mounted to the first plate.

25. The chromatography device according to any one of claims 16 to 23, wherein the flow distributor is arranged to reduce flow disturbances as fluid enters the tapered space from the inlet.

26. The chromatography device according to any one of claims 16 to 25 wherein the flow distributor comprises a first flow distributor and wherein the flow distributor arrangement further includes a second porous flow distributor disposed in the flow path between the tapered space and the porous media.

27. The chromatography device according to claim 26, wherein the tapered space includes a recess in the second porous flow distributor.

28. The chromatography device according to claim 26 or 27, wherein the first

porous flow distributor abuts the second porous flow distributor.

29. The chromatography device according to claim 26 or 27, wherein the first porous flow distributor is spaced from the second porous flow distributor.

30. The chromatography device according to any one of claims 26 to 29, wherein the second porous flow distributor is adapted to enhance uniform fluid flow.

31. The chromatography device according to any one of claims 26 to 30, wherein the second porous flow distributor is disposed in the porous medium module.

32. The chromatography device according to any one of claims 26 to 30, wherein the second porous flow distributor is disposed in the tapered space.

33. The chromatography device according to any one of claims 16 to 32, wherein the flow distributor arrangement is a first flow distributor arrangement and is disposed in the flow path between the porous media and the inlet, and wherein the chromatography device includes a second flow distributor arrangement disposed in the flow path between the porous media and the outlet.

34. The chromatography device according to claim 33, wherein the second flow distributor arrangement includes a tapered space and a porous flow distributor fluidly coupled to the tapered space, the tapered space of the second flow distributor arrangement being disposed in the flow path between the porous media and the outlet, wherein fluid flowing between the tapered space of the second flow distributor arrangement and the inlet passes through the porous flow distributor of the second flow distributor arrangement.

35. The chromatography device according to claim 34, wherein the tapered space of the second flow distributor arrangement is substantially free of structures.

36. The chromatography device according to claim 34 or 35 wherein the porous flow distributor of the second flow distributor arrangement comprises a first porous flow distributor and wherein the second flow distributor arrangement further includes a second porous flow distributor disposed in the flow path between the porous media and the outlet.

37. The chromatography device according to claim 36 wherein first porous flow distributor of the second flow distributor arrangement is mounted to the second plate and the second porous flow distributor of the second flow distributor arrangement is disposed in the porous medium module.

38. A chromatography device comprising:

an inlet and an outlet;

a porous medium module including a stack of porous media disposed in a flow path between the inlet and the outlet, the porous media having a flow area larger than a flow area of at least one of the inlet and the outlet; and

a flow distributor arrangement disposed in the flow path between the porous media and said one of the inlet and the outlet, the flow distributor arrangement including a tapered space and a porous flow distributor fluidly coupled to the tapered space, wherein the tapered space is disposed in the flow path between the porous media and said one of the inlet and the outlet and wherein the porous flow distributor is disposed in the flow path between the tapered space the porous media, the porous flow distributor being integrally secured to the porous medium module.

39. A chromatography device according to claim 38 wherein the tapered space is substantially free of structures.

40. A chromatography device according to claim 38 or 39 wherein the tapered space includes inner and outer tapered sections.

41. A chromatography device according to claim 40 wherein the tapered space includes a flat disposed between the inner and outer tapered sections and wherein the flow distributor arrangement includes supports extending from the flat toward the porous medium module.

42. A chromatography device according to any of claims 38-41 wherein the flow distributor arrangement includes another porous flow distributor disposed in the flow path between the tapered space and said one of the inlet or the outlet.

43. A chromatography device according to any of claims 38-41 wherein the flow distributor is the sole flow distributor of the flow distributor arrangement.

44. A flow distributor arrangement for distributing fluid flow in a chromatography device along a flow path between a first passage and a second passage, one of the passages having a larger flow area than the other passage, the flow distributor arrangement comprising:

a tapered space in the flow path between the first passage and the second passage, the tapered space including a first tapered section and a second tapered section disposed outwardly of the first tapered section; and

a porous flow distributor disposed in the flow path and fluidly coupled to the tapered space.

45. A flow distributor arrangement as claimed in claim 44 wherein the porous flow distributor is disposed in the fluid flow path between the tapered space and the first passage.

46. A flow distributor arrangement as claimed in claim 44 wherein the porous flow distributor is disposed in the fluid flow path between the tapered space and the second passage.

47. A flow distributor arrangement as claimed in any of claims 44-46 wherein the first and second tapered sections have different tapers.

48. A flow distributor arrangement as claimed in claim 47 wherein the first and second tapered sections respectively comprise inner and outer tapered sections, the inner tapered section having a steeper slope than the outer tapered section.

49. A flow distributor arrangement as claimed in any of claims 44-48 wherein the tapered space further includes a flat disposed between the first and second tapered sections.

50. A chromatography device comprising:

an inlet and an outlet defining a fluid flow path;

a porous medium module include a stack of porous media having a first end and a porous medium support supporting the first end of the stack of porous media, the porous medium module being disposed in the fluid flow path between the inlet and the outlet; and

a flow distributor arrangement disposed in the fluid flow path between the porous medium support and one of the inlet and the outlet, the flow distributor arrangement including a tapered space and a porous flow distributor fluidly coupled to the tapered space.

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PCT/US00/04785

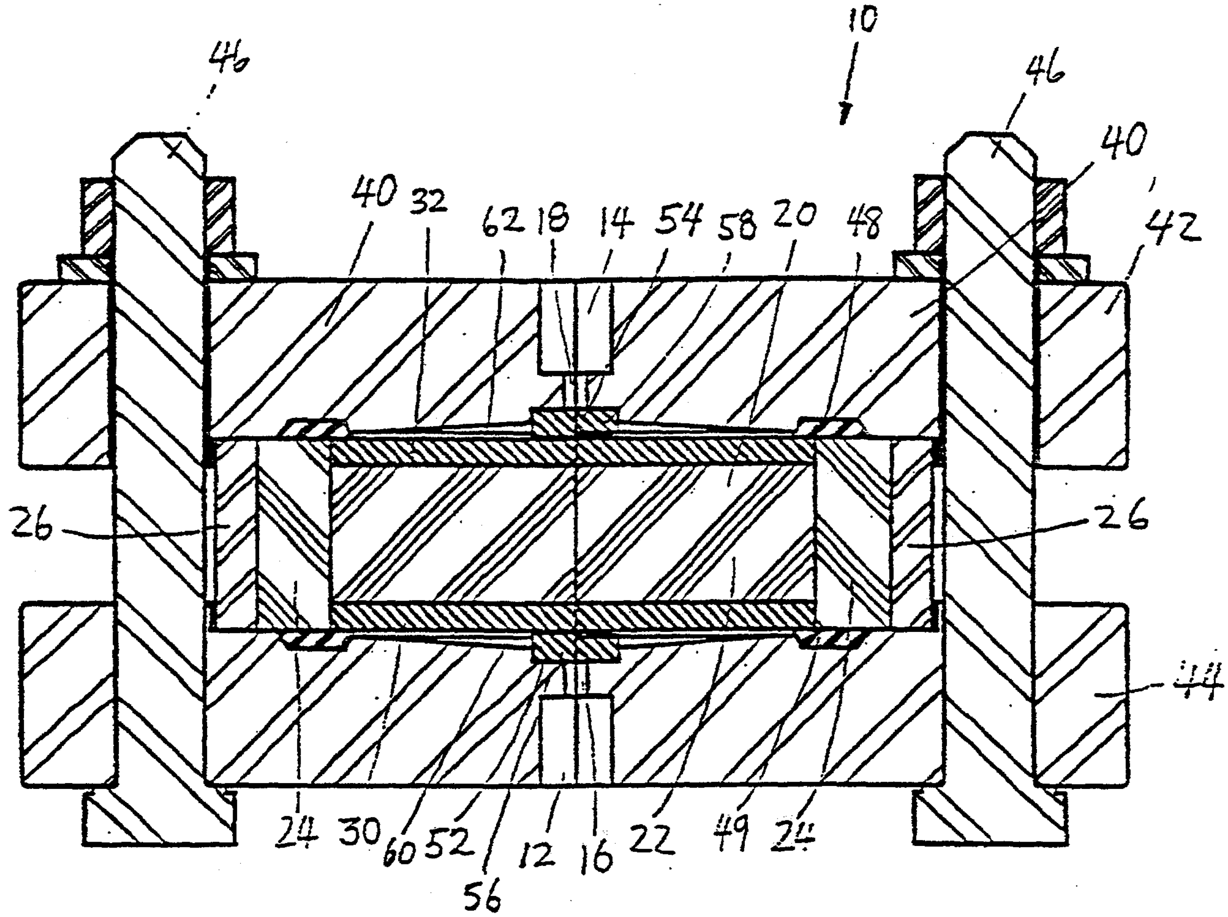

FIG. 1

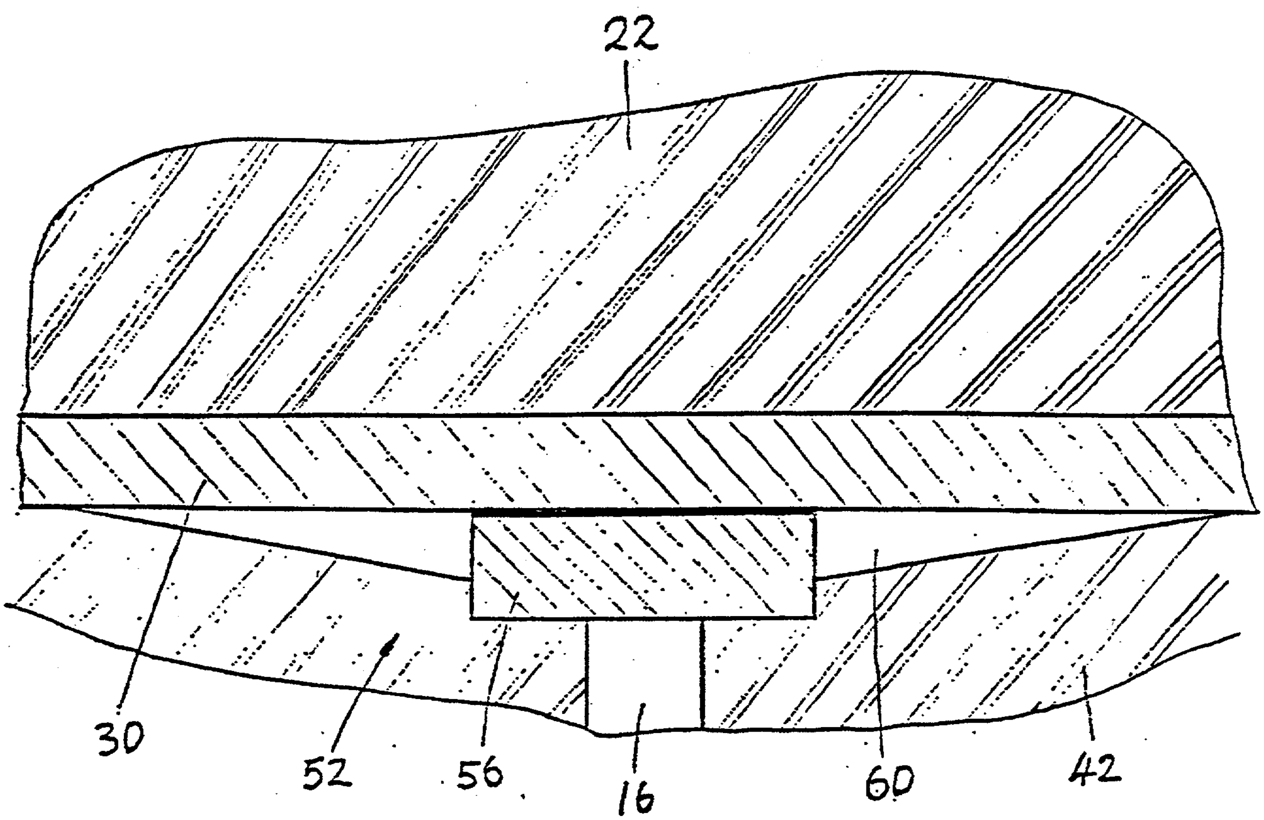

FIG. 2

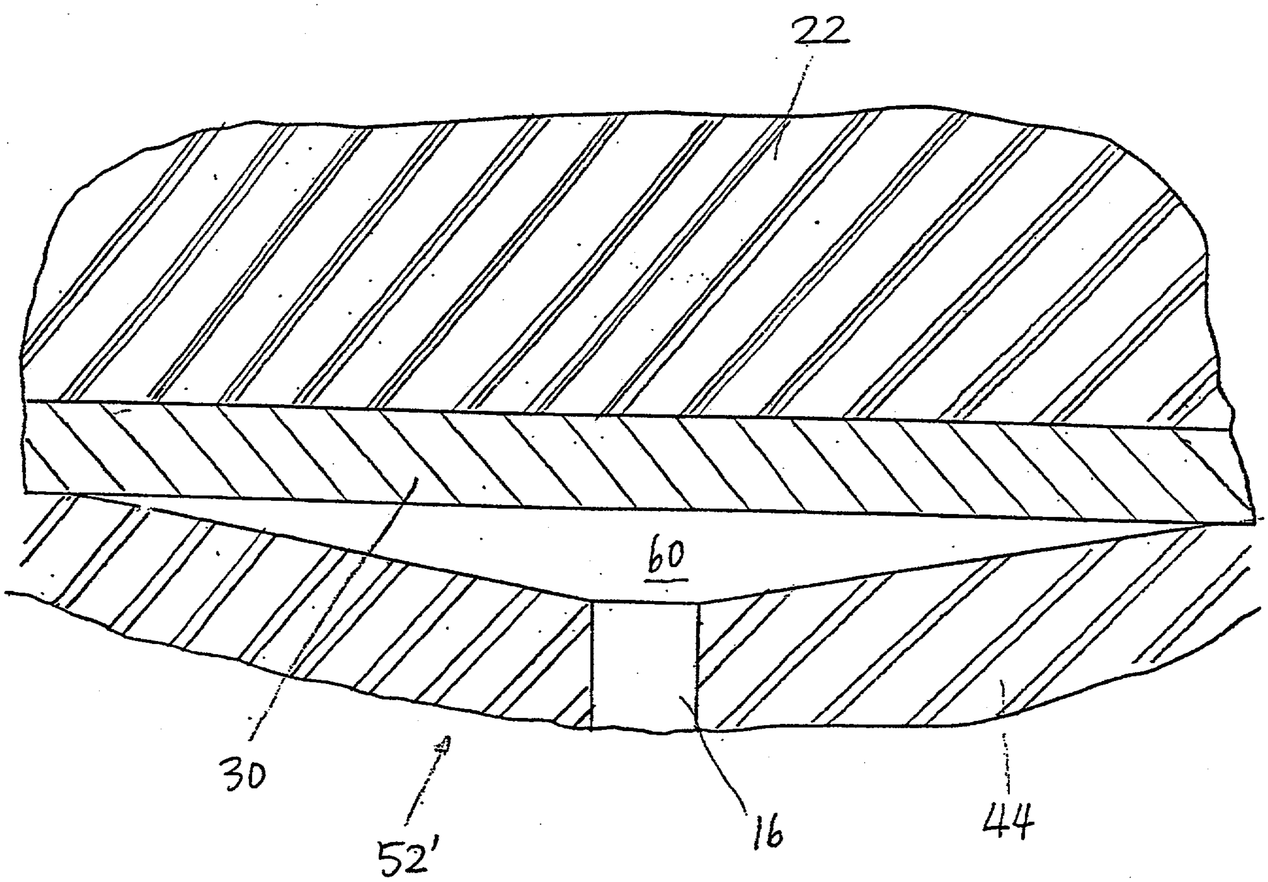

FIG. 3

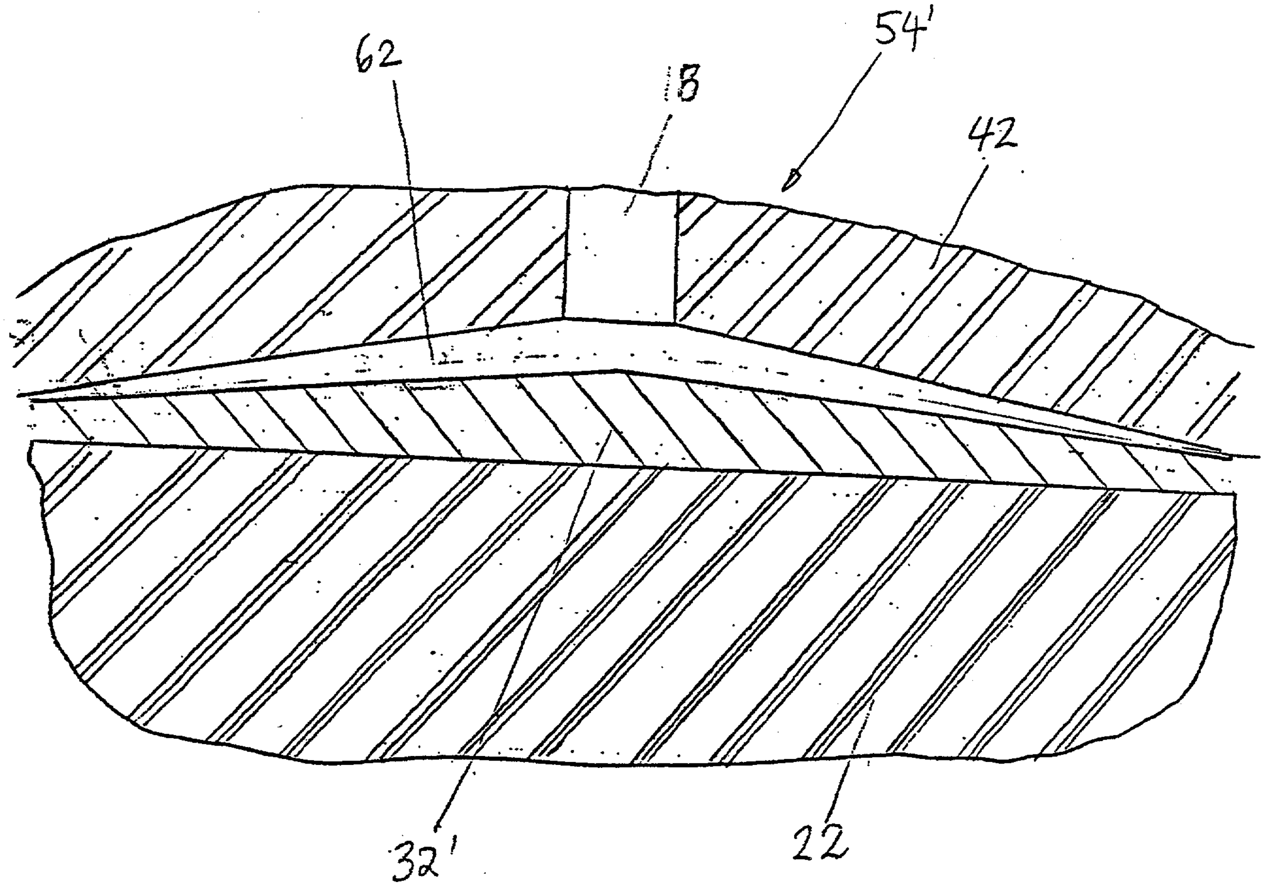

FIG. 4

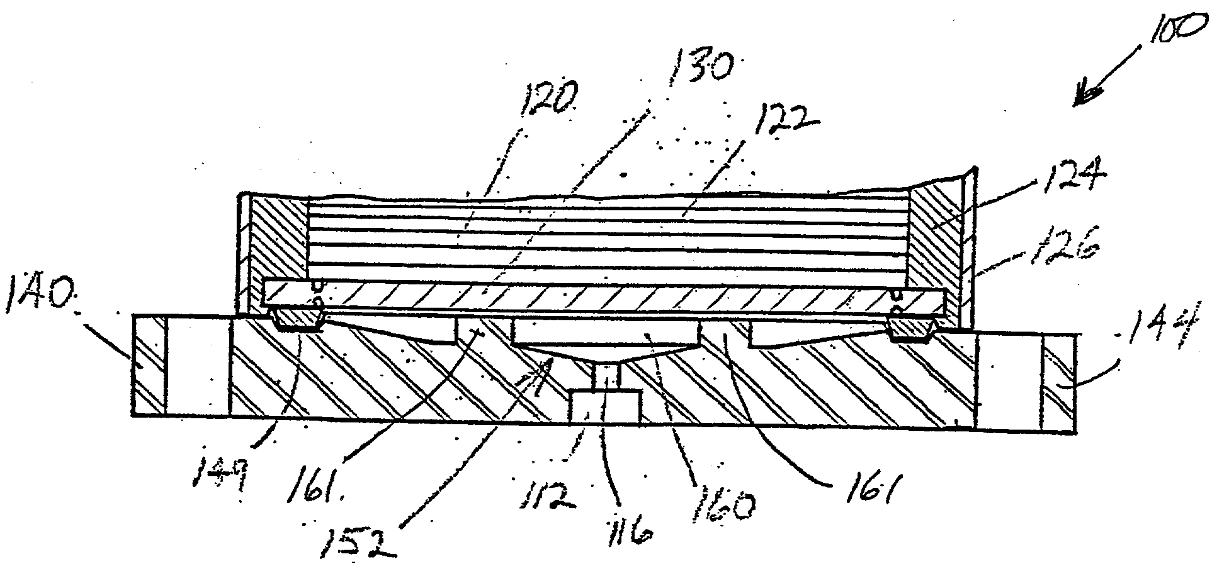

Figure 5

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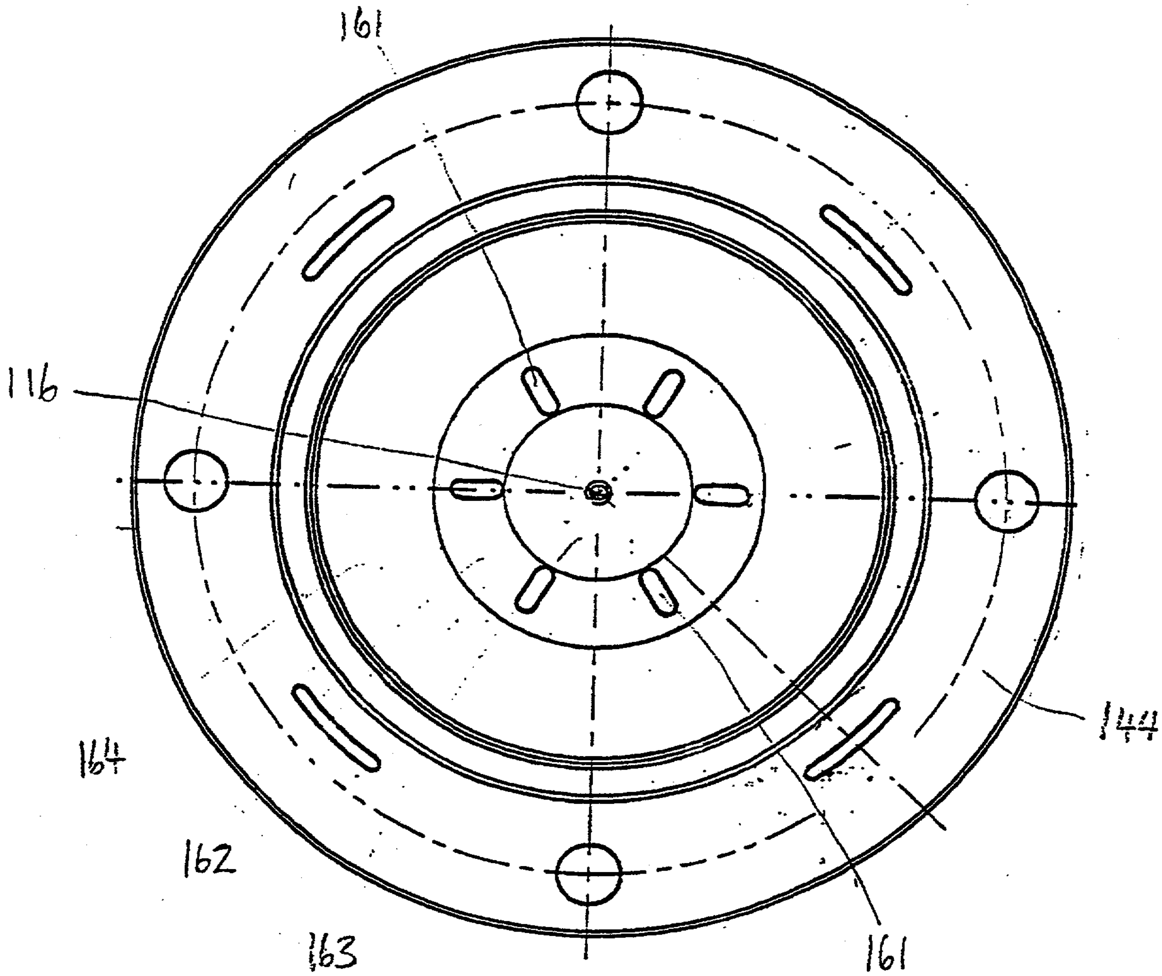


FIG. 6

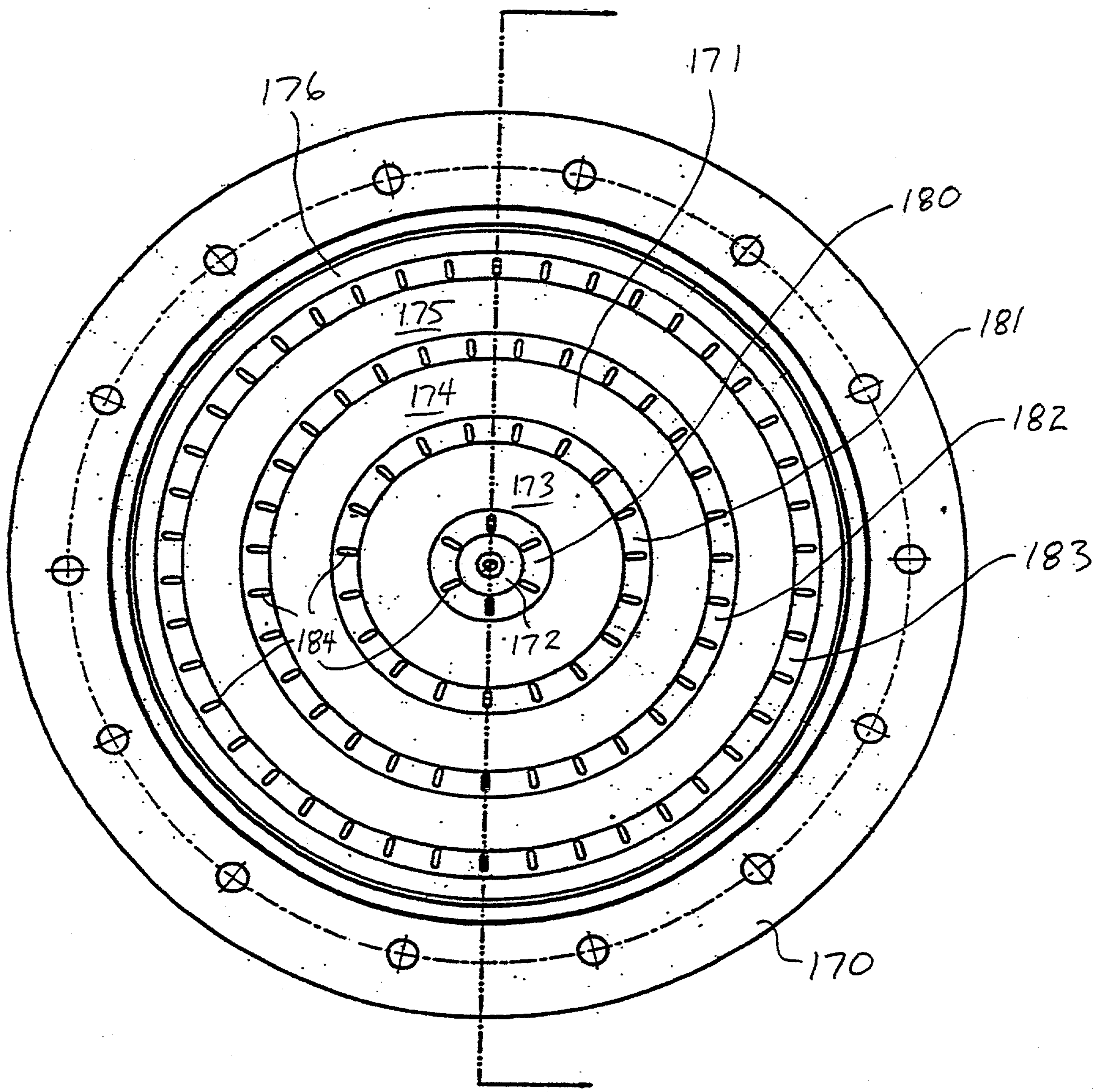
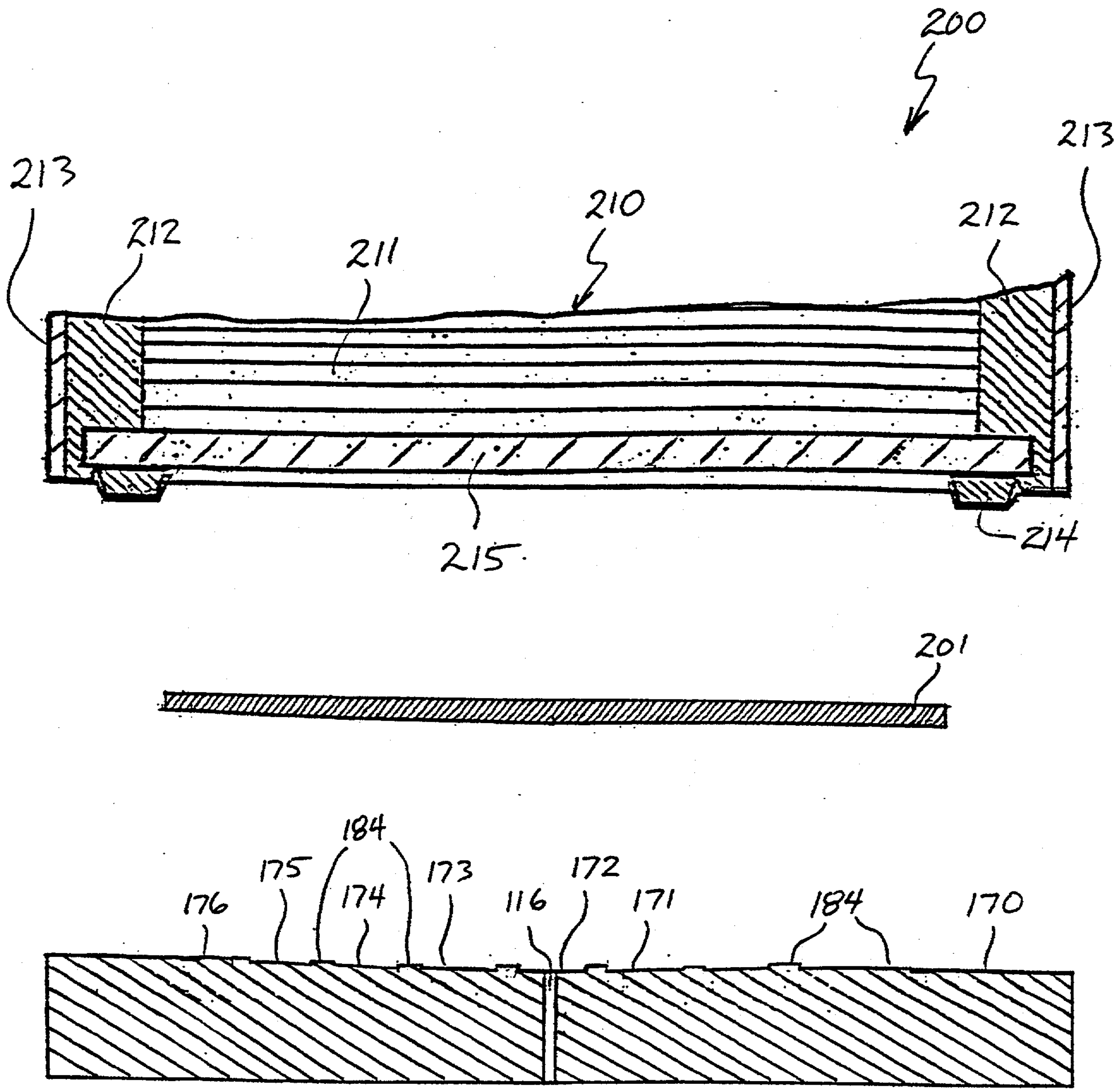


FIG. 7


200
213
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176
175
174
173
116
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170

FIG 8

#3

PATENT
Attorney Docket No. 440500

COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

This declaration is of the following type:

☐ original ☐ design ☐ supplemental
☒ national stage of PCT
☐ divisional ☐ continuation ☐ continuation-in-part

My residence, post office address, and citizenship are as stated below next to my name. I believe I am the original, first, and sole inventor *(if only one name is listed below)* or an original, first, and joint inventor *(if plural names are listed below)* of the subject matter which is claimed and for which a patent is sought on the invention entitled:

CHROMATOGRAPHY DEVICES AND FLOW DISTRIBUTOR ARRANGEMENTS USED IN CHROMATOGRAPHY DEVICES

the specification of which:

☐ is attached hereto.
☐ was filed on as Application No. and was amended on *(if applicable)*.
☐ was filed by Express Mail No. *as Application No. not known yet*, and was amended on *(if applicable)*.
☒ was filed on February 25, 2000 as PCT International Application No. PCT/US00/04785 and was entered in the U.S. national phase as application No. 09/914,166.

I state that I have reviewed and understand the contents of the specification identified above, including the claim(s), as amended by any amendment referred to above.

I acknowledge the duty to disclose information that is material to the patentability of the application identified above in accordance with 37 CFR 1.56.

I claim foreign priority benefits under 35 USC 119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate or 365(a) of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent, utility model, design registration, or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter and having a filing date before that of the application(s) from which the benefit of priority is claimed.

PRIOR FOREIGN PATENT, UTILITY MODEL, AND DESIGN REGISTRATION APPLICATIONS						
COUNTRY	PRIOR FOREIGN APPLICATION NO.	DATE OF FILING (day,month,year)	PRIORITY CLAIMED			
				YES		NO
				YES		NO
				YES		NO

I claim the benefit pursuant to 35 USC 119(e) of the following United States provisional patent application(s):

PRIOR U.S. PROVISIONAL PATENT APPLICATIONS, BENEFIT CLAIMED UNDER 35 USC 119(e)	
APPLICATION NO.	DATE OF FILING (day,month,year)
60/121,701	25 February 1999
60/168,750	6 December 1999

I claim the benefit pursuant to 35 USC 120 of any United States patent application(s) or PCT international application(s) designating the United States of America listed below and, insofar as the subject matter of each of the claims of this patent application is not disclosed in the prior patent application(s) in the manner provided by the first paragraph of 35 USC 112, I acknowledge the duty to disclose material information as defined in 37 CFR 1.56 effective between the filing date of the prior patent application(s) and the national or PCT international filing date of this patent application.

PRIOR U.S. PATENT APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S., BENEFIT CLAIMED UNDER 35 USC 120					
U.S. PATENT APPLICATIONS			Status *(check one)*		
U.S. APPLICATION NO.	U.S. FILING DATE		PATENTED	PENDING	ABANDONED
1.					
2.					
3.					
PCT APPLICATIONS DESIGNATING THE U.S.			Status *(check one)*		
PCT APPLICATION NO.	PCT FILING DATE (day,month,year)	U.S. APPLICATION NOS. ASSIGNED (if any)	PATENTED	PENDING	ABANDONED
4.					
5.					
6.					

DETAILS OF FOREIGN APPLICATIONS FROM WHICH PRIORITY CLAIMED UNDER 35 USC 119 FOR ABOVE LISTED U.S./PCT APPLICATIONS				
ABOVE APPLICATION. NO.	COUNTRY	APPLICATION NO.	DATE OF FILING (day,month,year)	DATE OF ISSUE (day,month,year)
1.				
2.				
3.				
4.				
5.				
6.				

#3

PATENT
Attorney Docket No. 440500

COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

This declaration is of the following type:

☐ original ☐ design ☐ supplemental
☒ national stage of PCT
☐ divisional ☐ continuation ☐ continuation-in-part

My residence, post office address, and citizenship are as stated below next to my name. I believe I am the original, first, and sole inventor *(if only one name is listed below)* or an original, first, and joint inventor *(if plural names are listed below)* of the subject matter which is claimed and for which a patent is sought on the invention entitled:

CHROMATOGRAPHY DEVICES AND FLOW DISTRIBUTOR ARRANGEMENTS USED IN CHROMATOGRAPHY DEVICES

the specification of which:

☐ is attached hereto.
☐ was filed on as Application No. and was amended on *(if applicable)*.
☐ was filed by Express Mail No. *as Application No. not known yet*, and was amended on *(if applicable)*.
☒ was filed on February 25, 2000 as PCT International Application No. PCT/US00/04785 and was entered in the U.S. national phase as application No. 09/914,166.

I state that I have reviewed and understand the contents of the specification identified above, including the claim(s), as amended by any amendment referred to above.

I acknowledge the duty to disclose information that is material to the patentability of the application identified above in accordance with 37 CFR 1.56.

I claim foreign priority benefits under 35 USC 119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate or 365(a) of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent, utility model, design registration, or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter and having a filing date before that of the application(s) from which the benefit of priority is claimed.

PRIOR FOREIGN PATENT, UTILITY MODEL, AND DESIGN REGISTRATION APPLICATIONS						
COUNTRY	PRIOR FOREIGN APPLICATION NO.	DATE OF FILING (day,month,year)	PRIORITY CLAIMED			
				YES		NO
				YES		NO
				YES		NO

In re Appln. of Hurwitz et al.
Attorney Docket No. 440500

I claim the benefit pursuant to 35 USC 119(e) of the following United States provisional patent application(s):

PRIOR U.S. PROVISIONAL PATENT APPLICATIONS, BENEFIT CLAIMED UNDER 35 USC 119(e)	
APPLICATION NO.	DATE OF FILING (day,month,year)
60/121,701	25 February 1999
60/168,750	6 December 1999

I claim the benefit pursuant to 35 USC 120 of any United States patent application(s) or PCT international application(s) designating the United States of America listed below and, insofar as the subject matter of each of the claims of this patent application is not disclosed in the prior patent application(s) in the manner provided by the first paragraph of 35 USC 112, I acknowledge the duty to disclose material information as defined in 37 CFR 1.56 effective between the filing date of the prior patent application(s) and the national or PCT international filing date of this patent application.

PRIOR U.S. PATENT APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S., BENEFIT CLAIMED UNDER 35 USC 120					
U.S. PATENT APPLICATIONS			Status *(check one)*		
U.S. APPLICATION NO.	U.S. FILING DATE		PATENTED	PENDING	ABANDONED
1.					
2.					
3.					
PCT APPLICATIONS DESIGNATING THE U.S.			Status *(check one)*		
PCT APPLICATION NO.	PCT FILING DATE (day,month,year)	U.S. APPLICATION NOS. ASSIGNED (if any)	PATENTED	PENDING	ABANDONED
4.					
5.					
6.					

DETAILS OF FOREIGN APPLICATIONS FROM WHICH PRIORITY CLAIMED UNDER 35 USC 119 FOR ABOVE LISTED U.S./PCT APPLICATIONS				
ABOVE APPLICATION. NO.	COUNTRY	APPLICATION NO.	DATE OF FILING (day,month,year)	DATE OF ISSUE (day,month,year)
1.				
2.				
3.				
4.				
5.				
6.				

In re Appln. of Hurwitz et al.
Attorney Docket No. 440500

As a named inventor, I appoint the following registered practitioner(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith: Customer Number 23548.

23548

PATENT TRADEMARK OFFICE

I further direct that correspondence concerning this application be directed to Customer Number 23548.

23548

PATENT TRADEMARK OFFICE

I declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first inventor: Mark F. HURWITZ

Inventor's signature ______________________________

Date ____________________ Country of Citizenship: USA

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Post Office Address: 345 Snyderville Road
Ithaca, NY 14850

Full name of second joint inventor, if any: Thomas SORENSEN

Inventor's signature ______________________________

Date ____________________ Country of Citizenship: US

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Full name of third joint inventor, if any: John STREMPEL

Inventor's signature ______________________________

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4-00

Full name of fourth joint inventor, if any Thomas FENDYA

Inventor's signature Thomas J. Fendya

Date Nov. 19, 2001 Country of Citizenship: USA

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In re Appln. of Hurwitz et al.
Attorney Docket No. 440500

As a named inventor, I appoint the following registered practitioner(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith: Customer Number 23548.

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1-00

Full name of sole or first inventor: Mark F. HURWITZ

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3-CD

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